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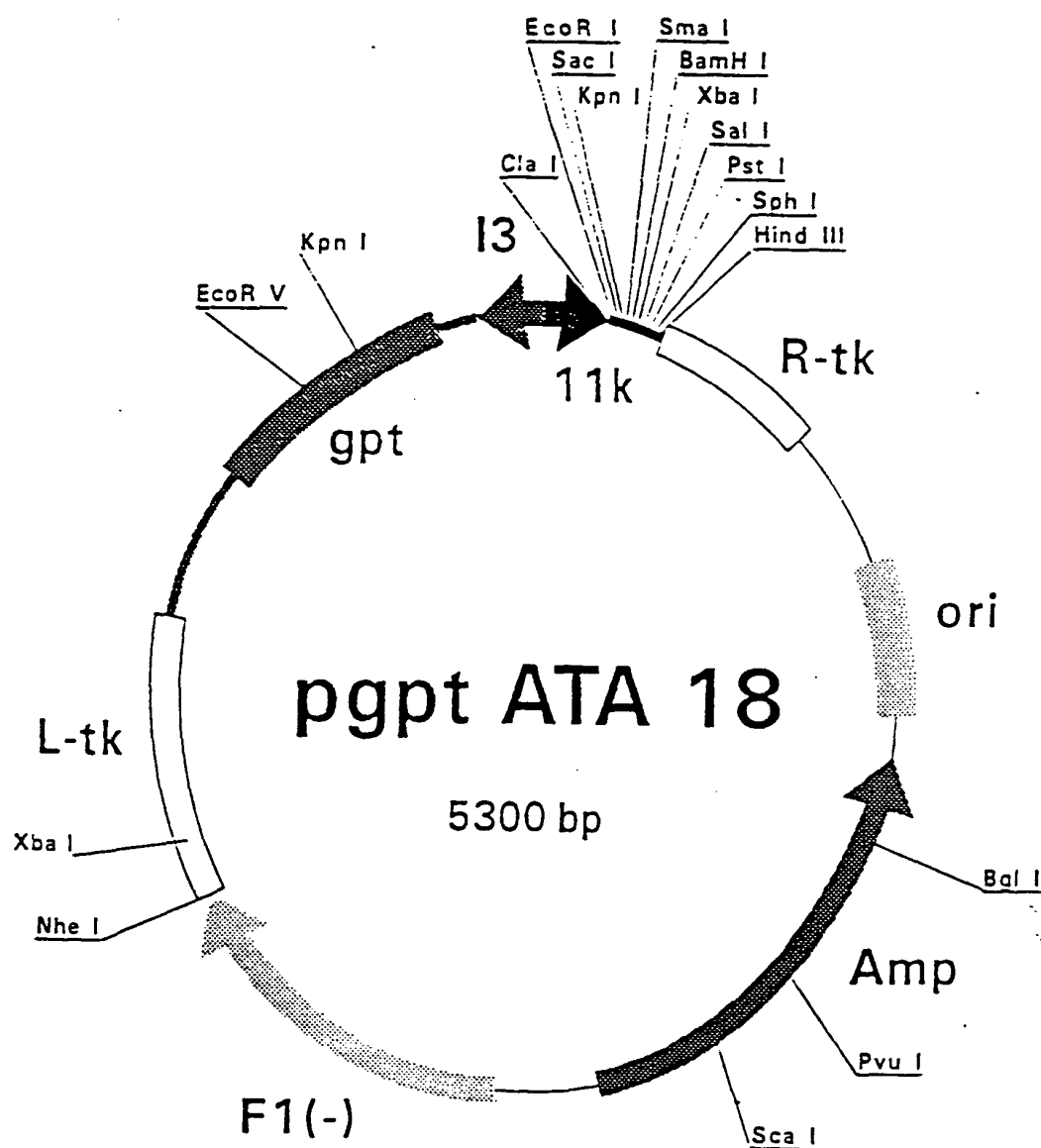


FIGURE 1

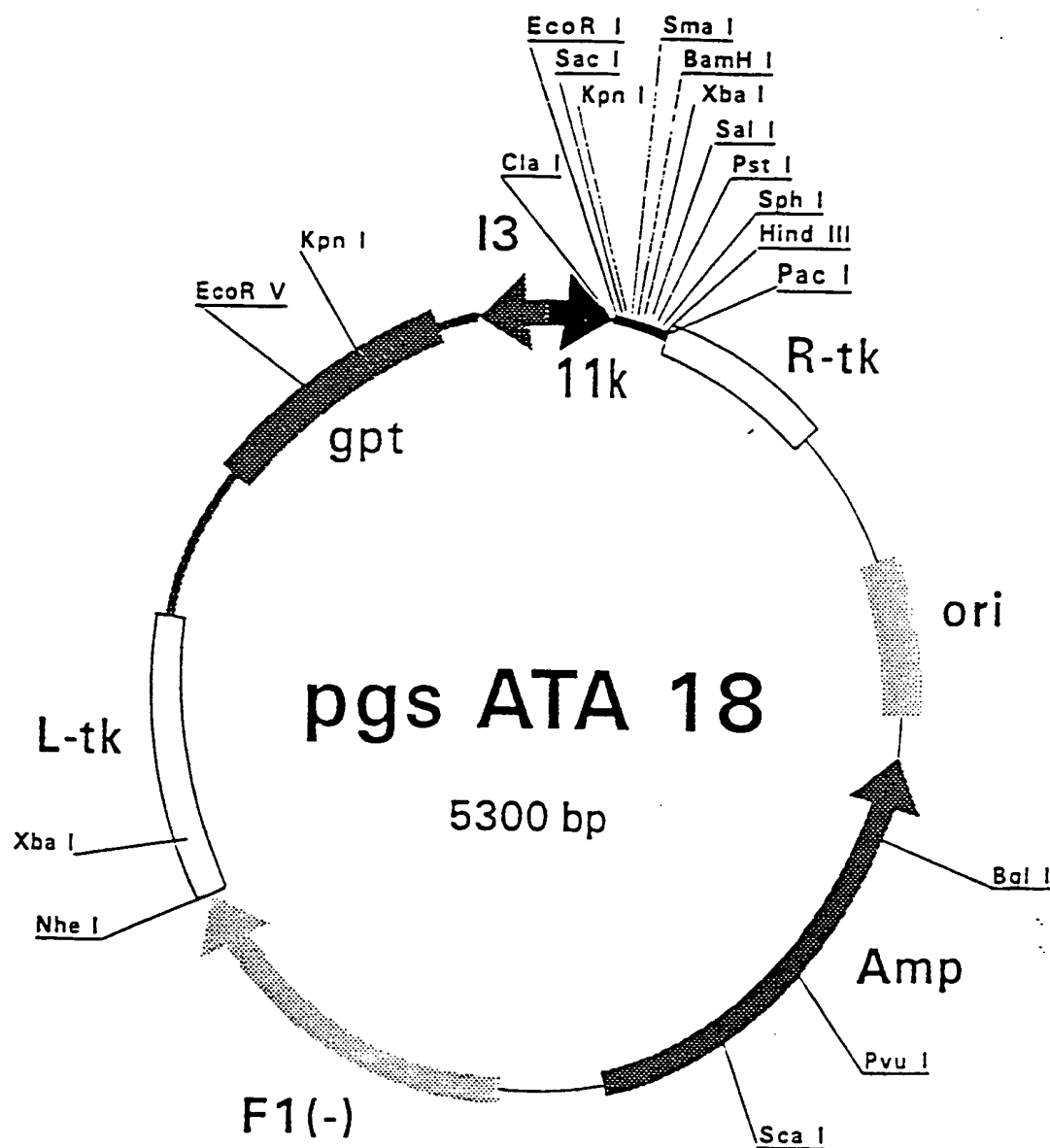


FIGURE 2

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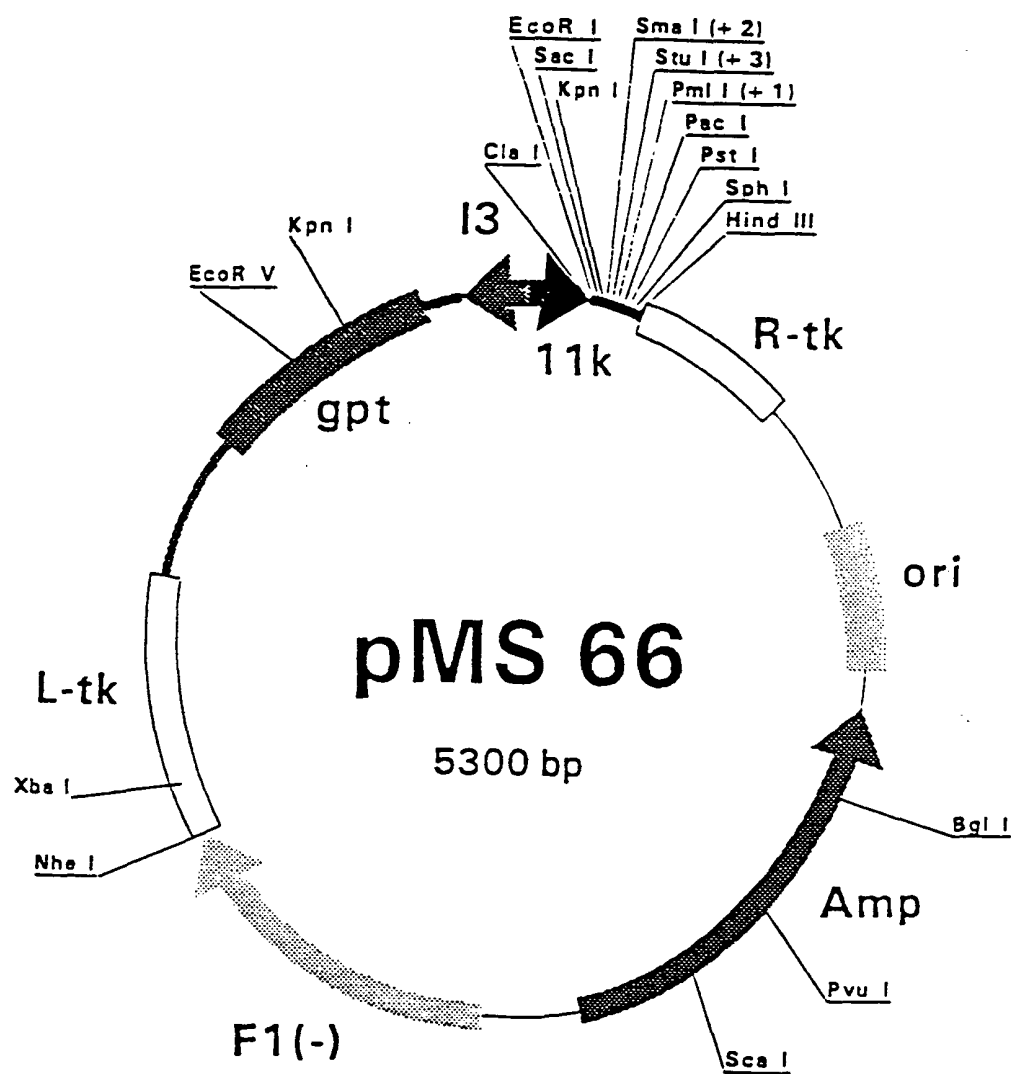


FIGURE 3

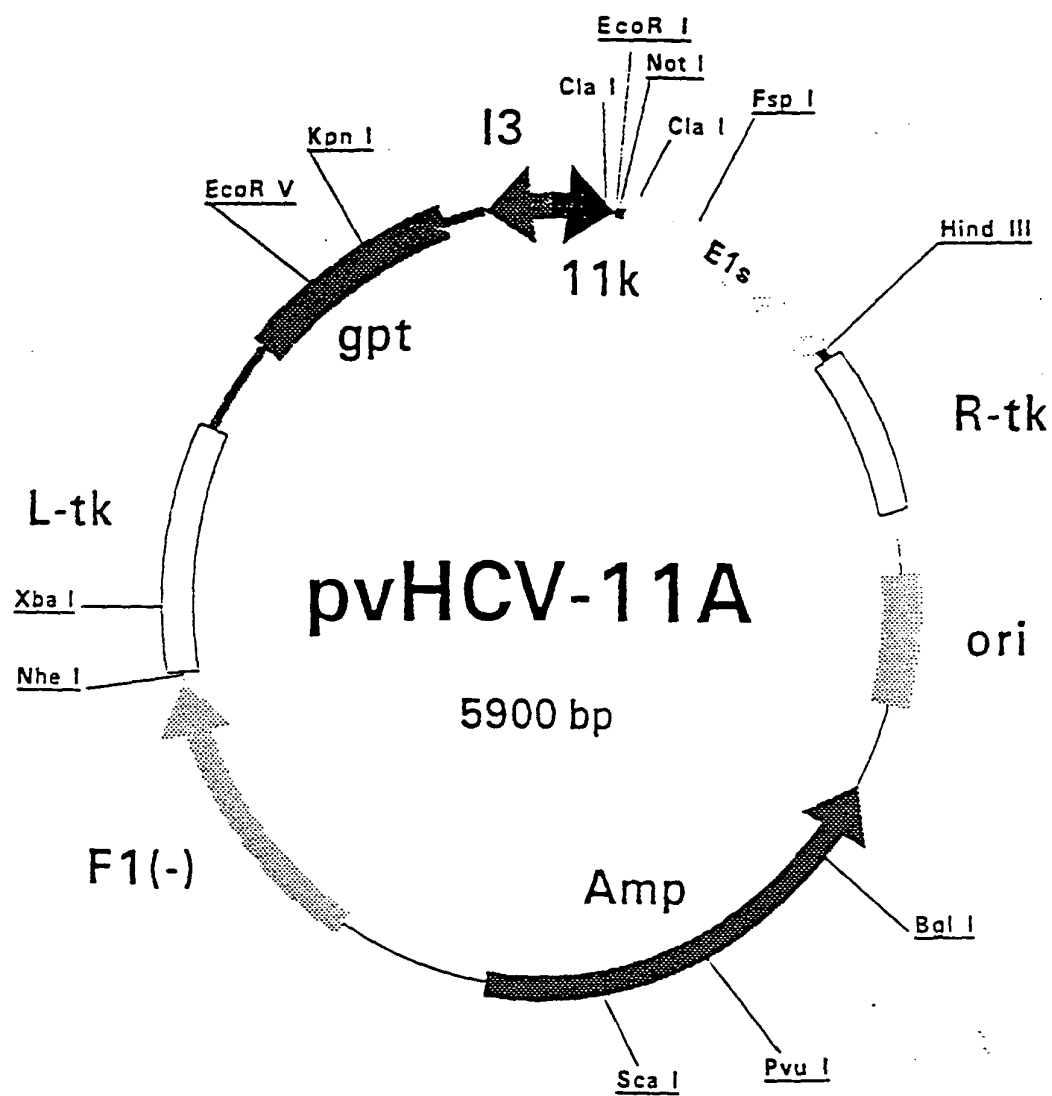


FIGURE 4

Anti-E1 levels in NON-responders to IFN treatment

Series 1

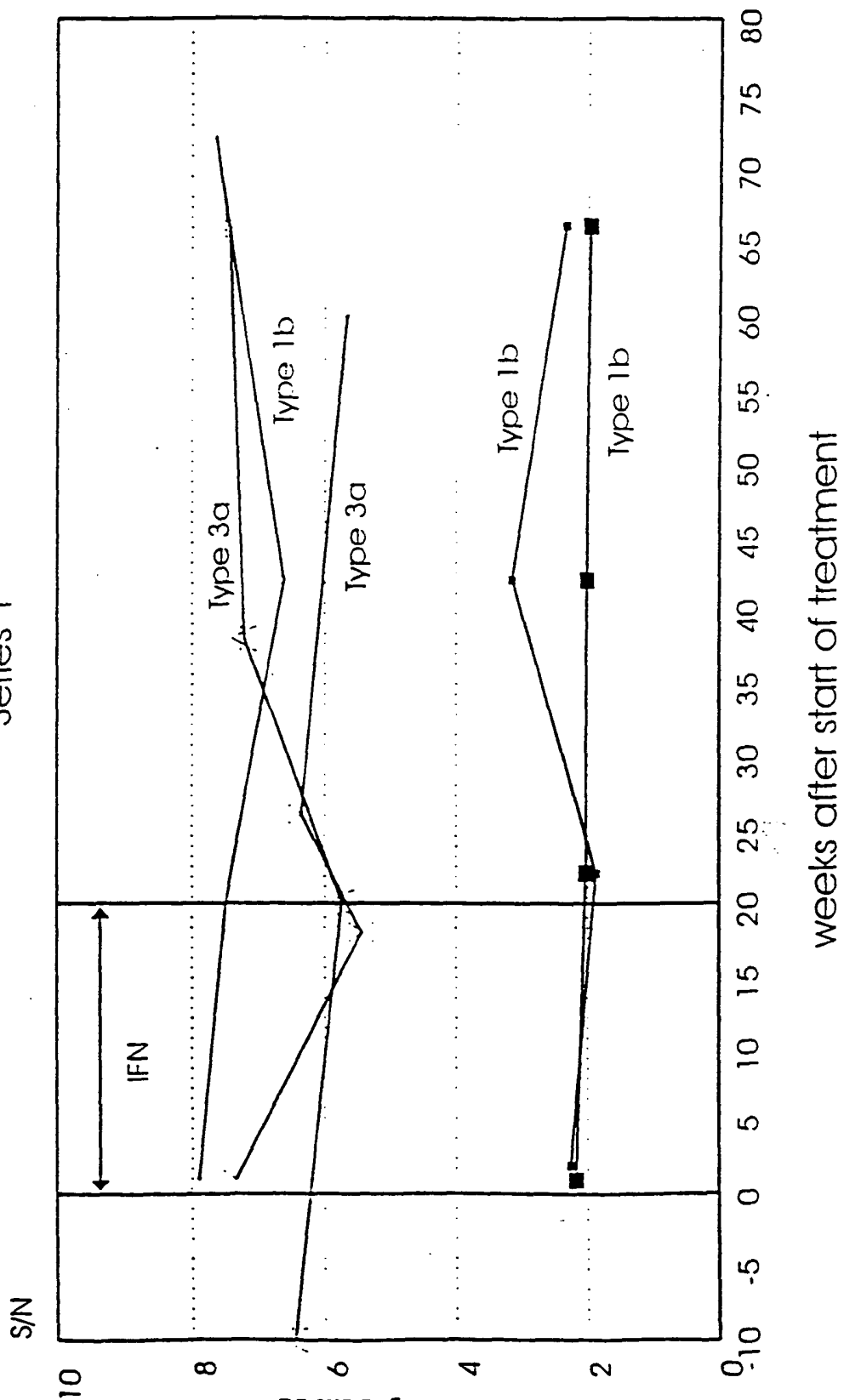
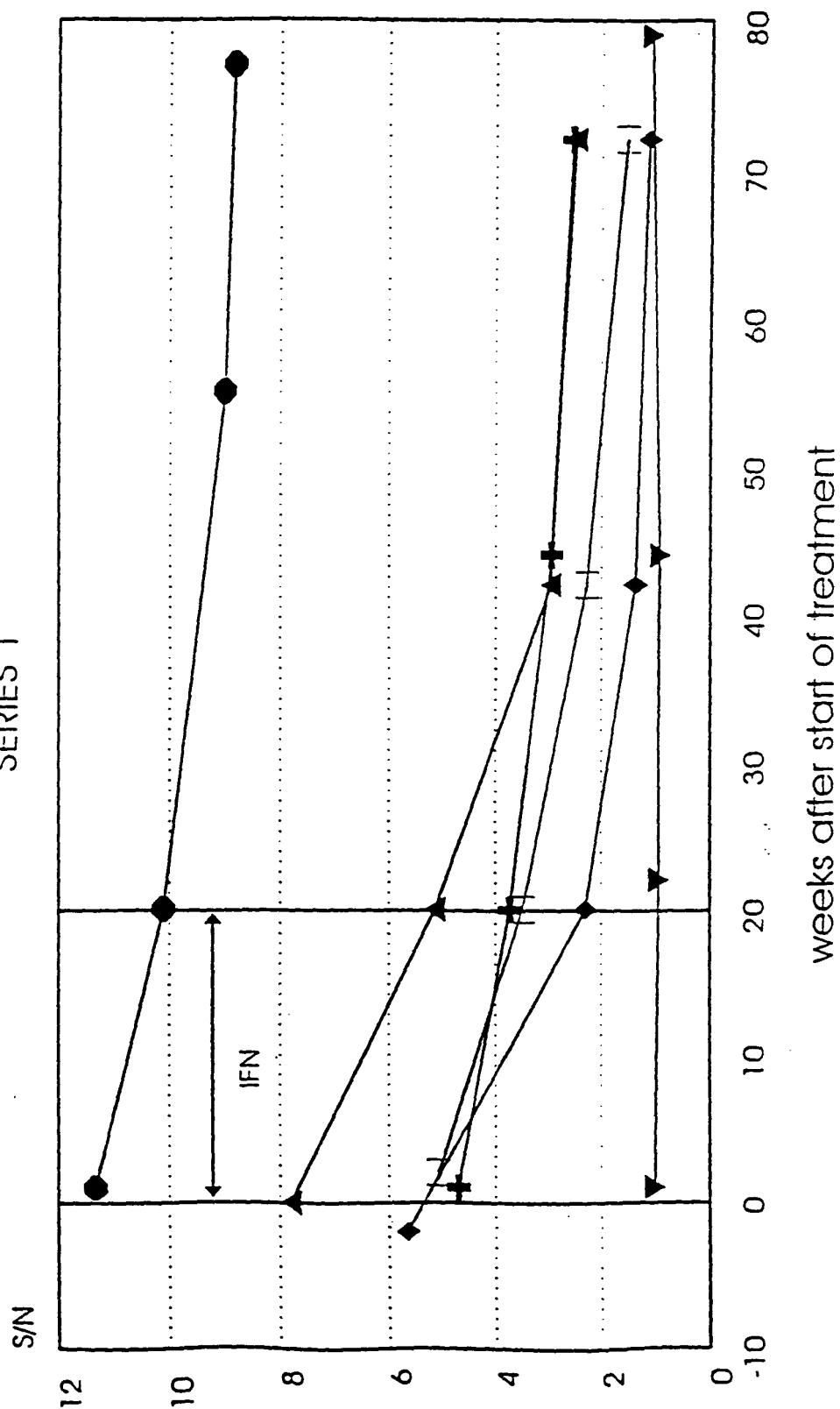


FIGURE 5

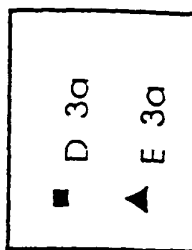
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Anti-E1 levels in RESPONDERS to IFN treatment

SERIES 1



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Anti-E1 levels in patients with COMPLETE response to IFN

SERIES 2

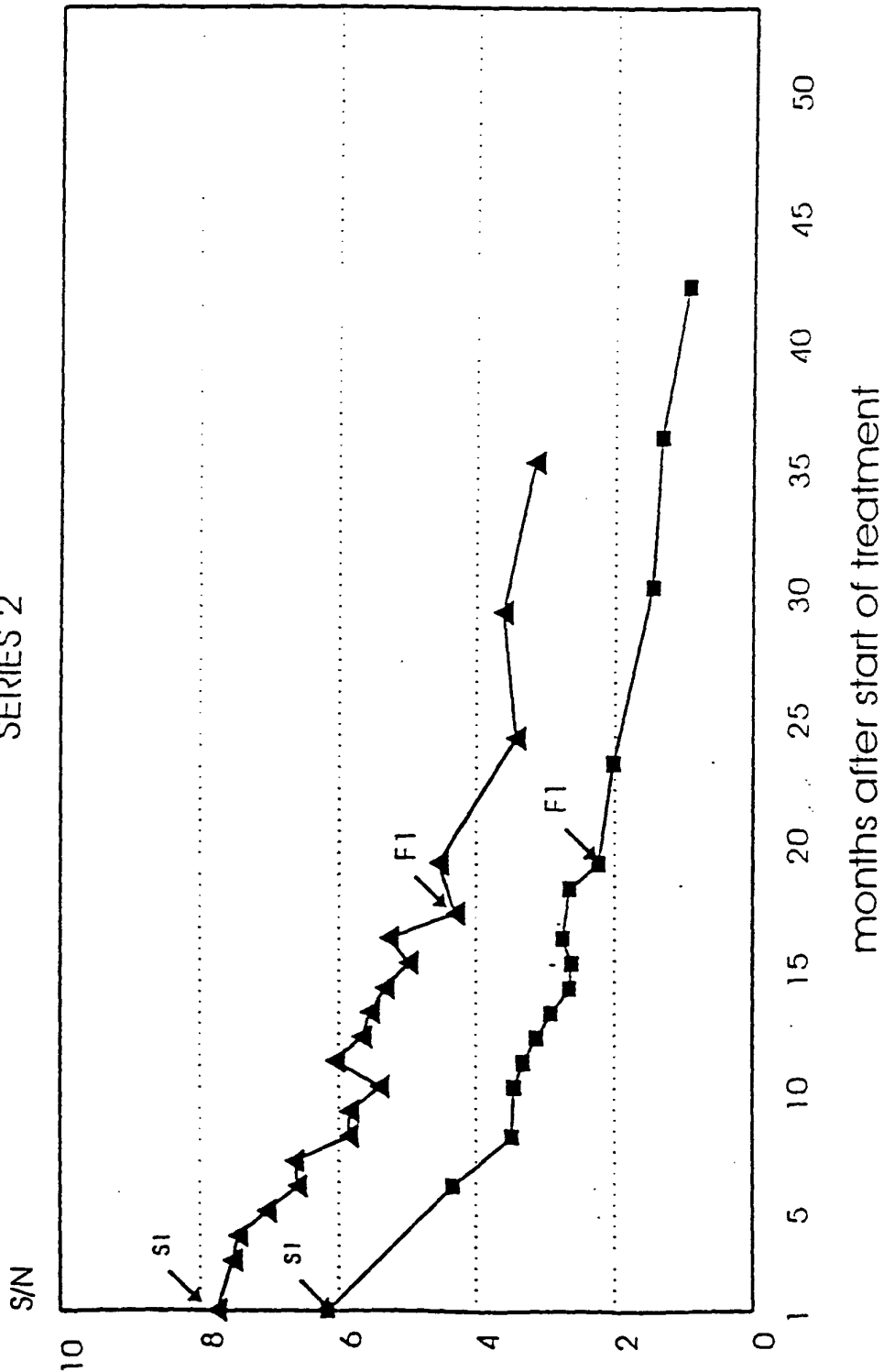


FIGURE 7

Anti-E1 levels in INCOMPLETE responders to IFN treatment

SERIES 2

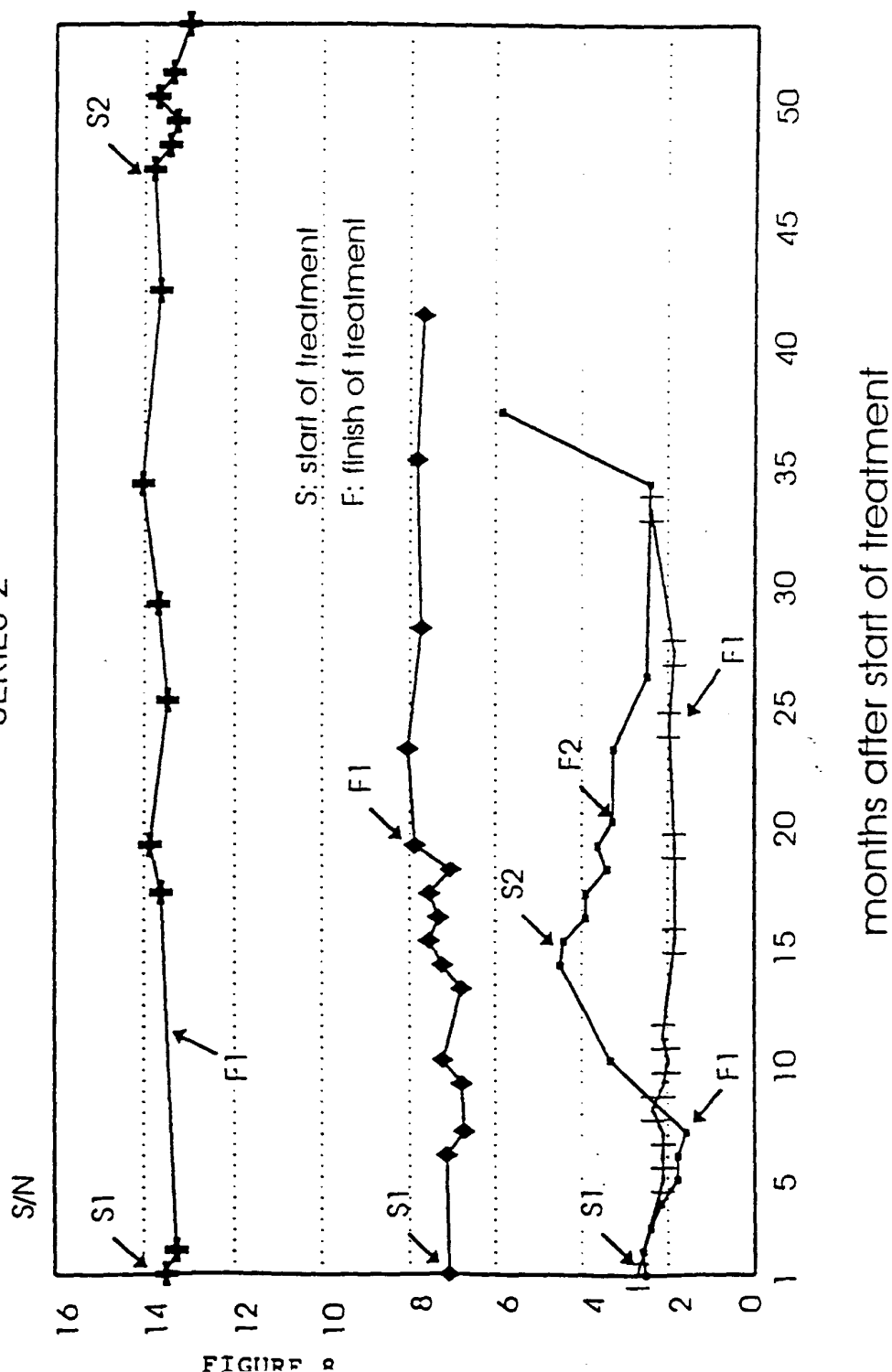
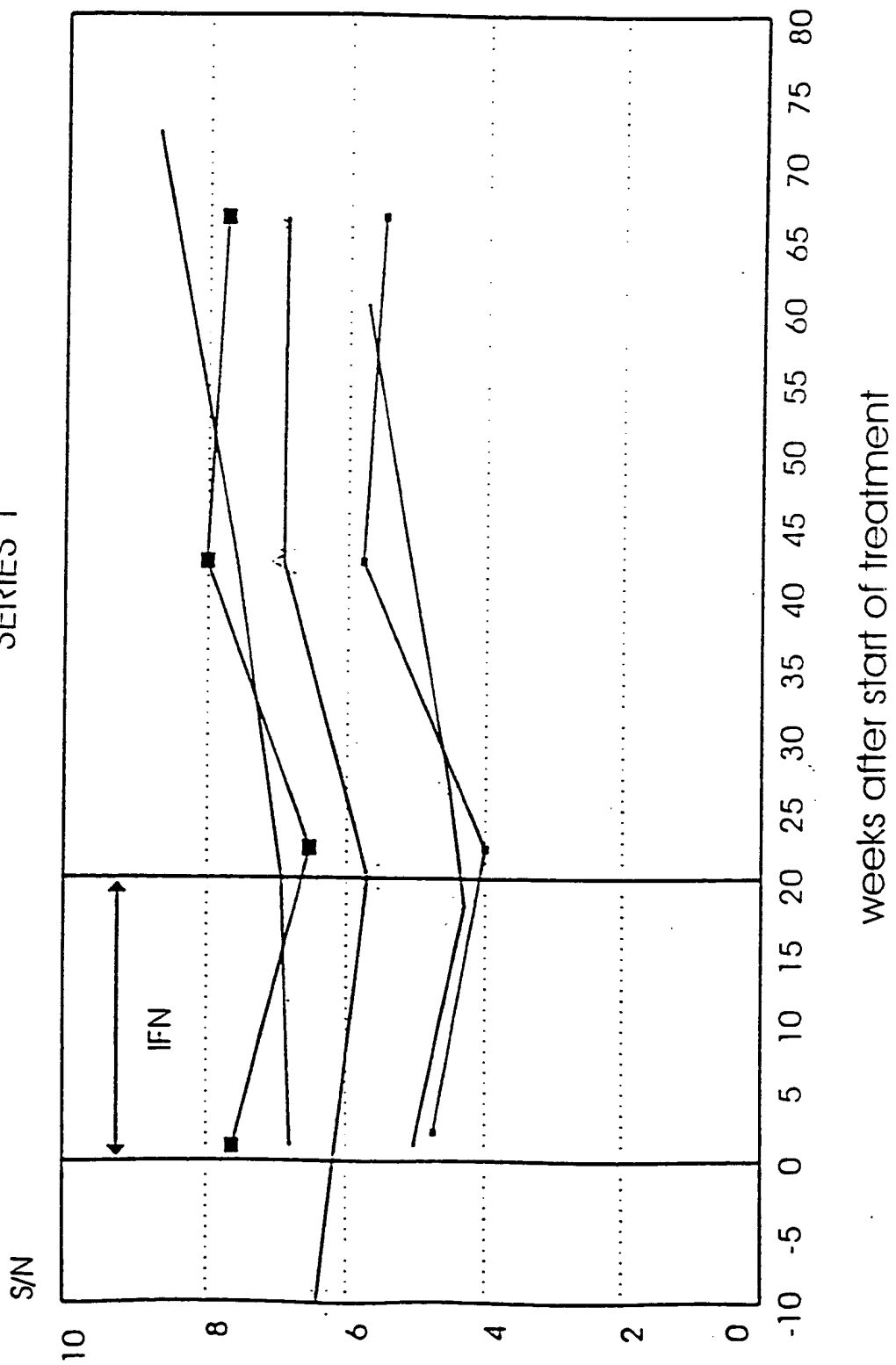


FIGURE 2

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Anti-E2 levels in NON-RESPONDERS to IFN treatment

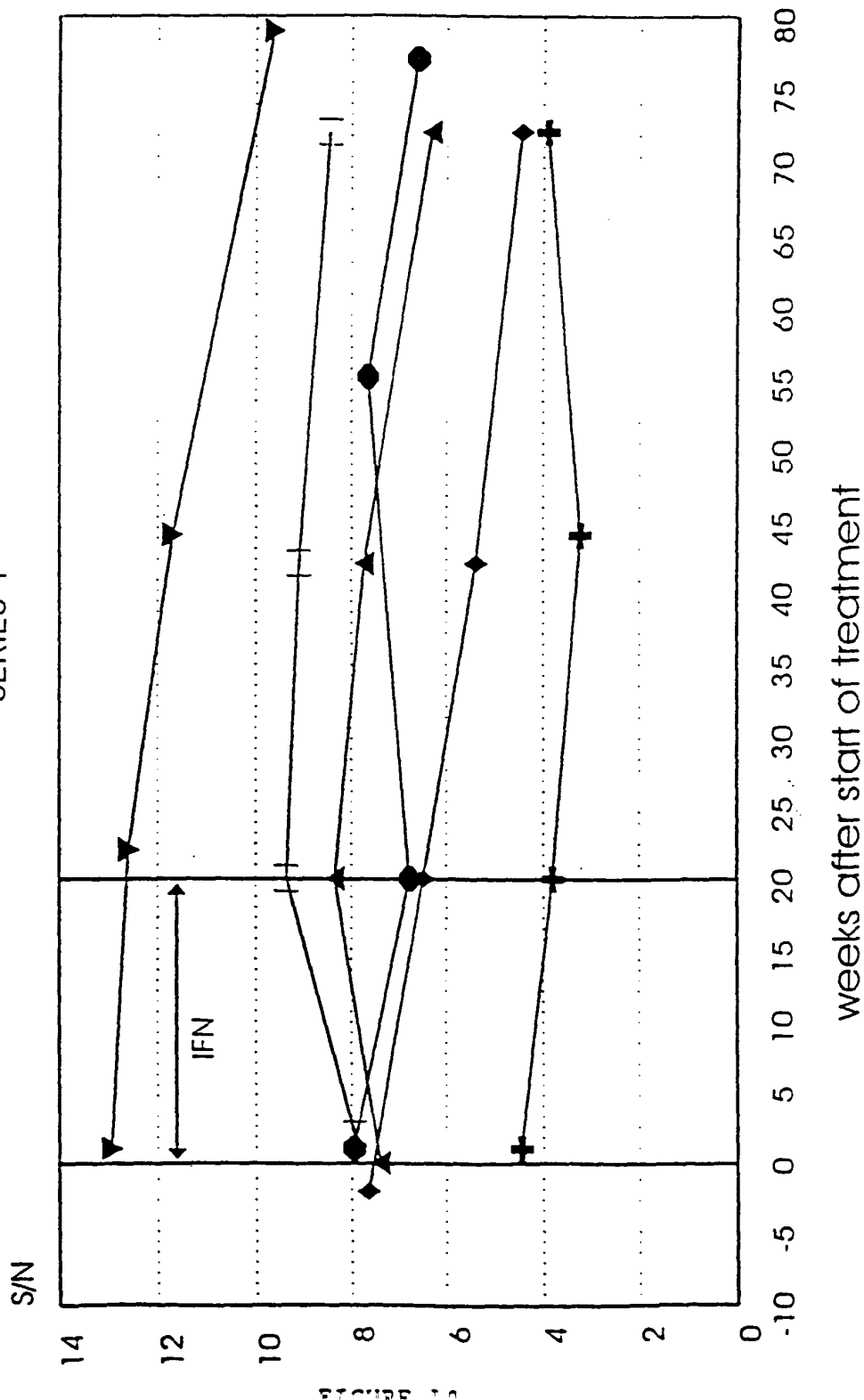
SERIES 1



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Anti-E2 levels in RESPONDERS to IFN treatment

SERIES 1



Anti-E2 levels in INCOMPLETE responders to IFN treatment

SERIES 2

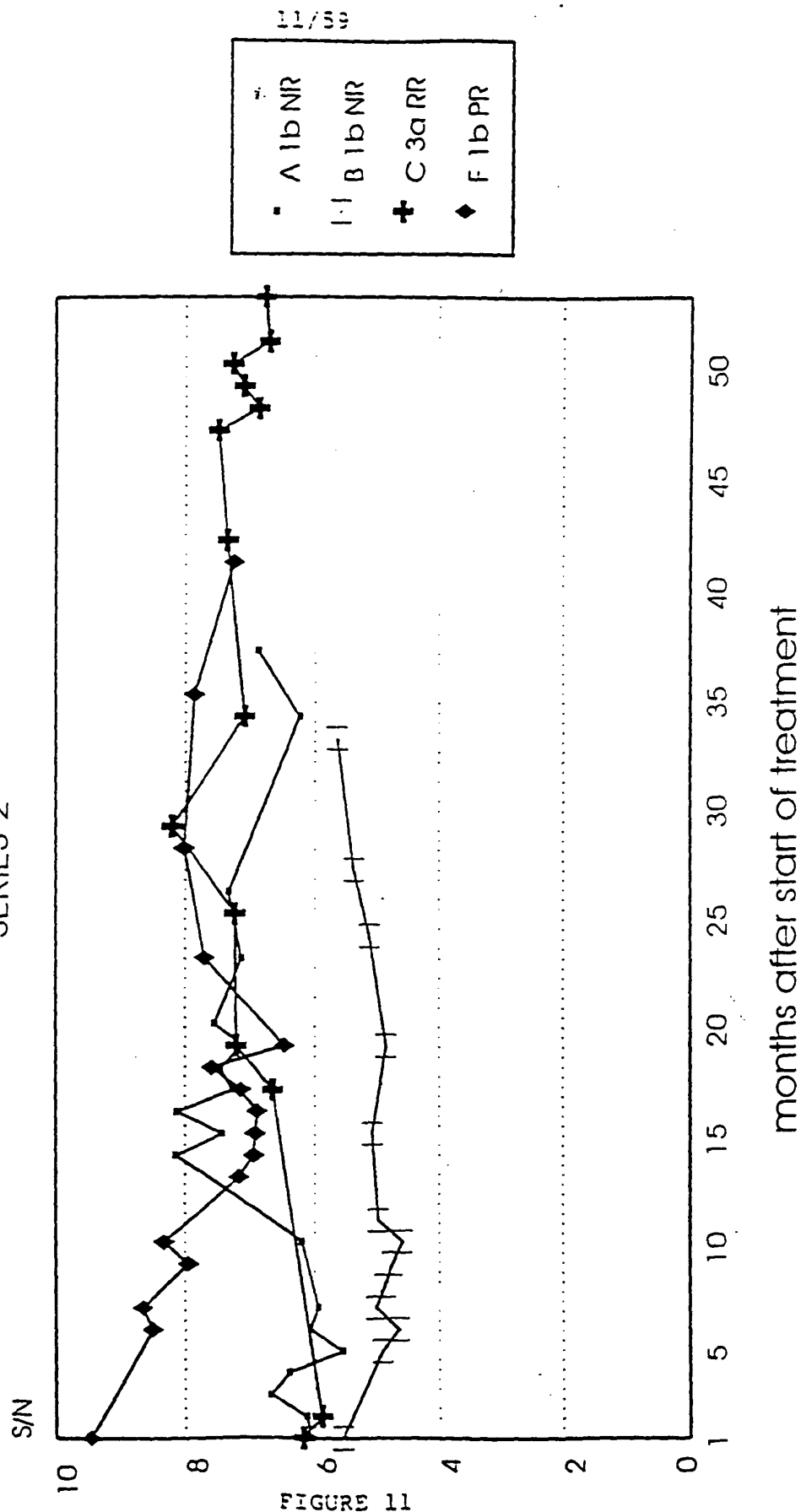


FIGURE 11

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Anti-E2 levels in COMPLETE responders to IFN treatment

SERIES 2

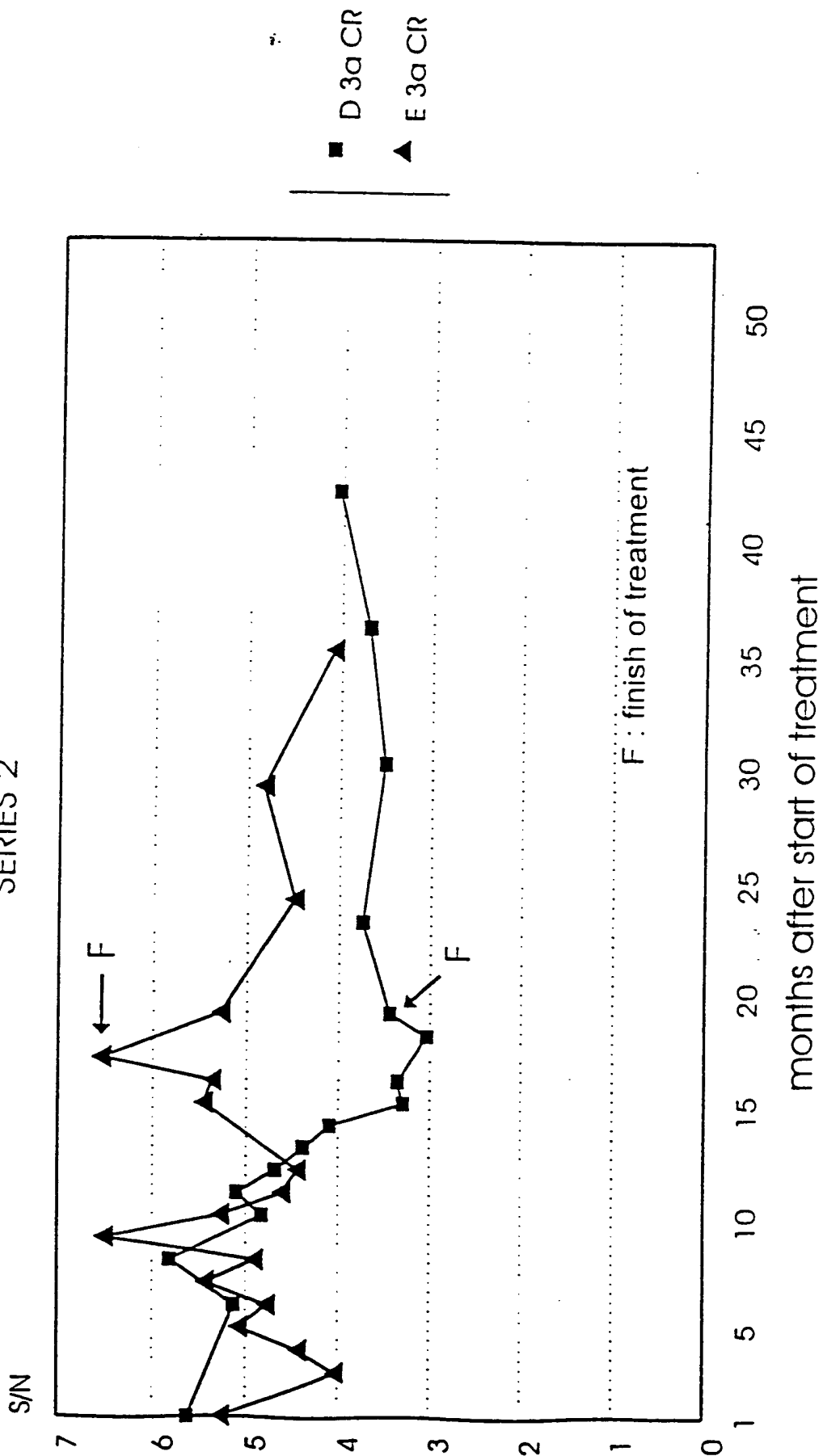


FIGURE 12

Human anti-E1 reactivity competed with peptides

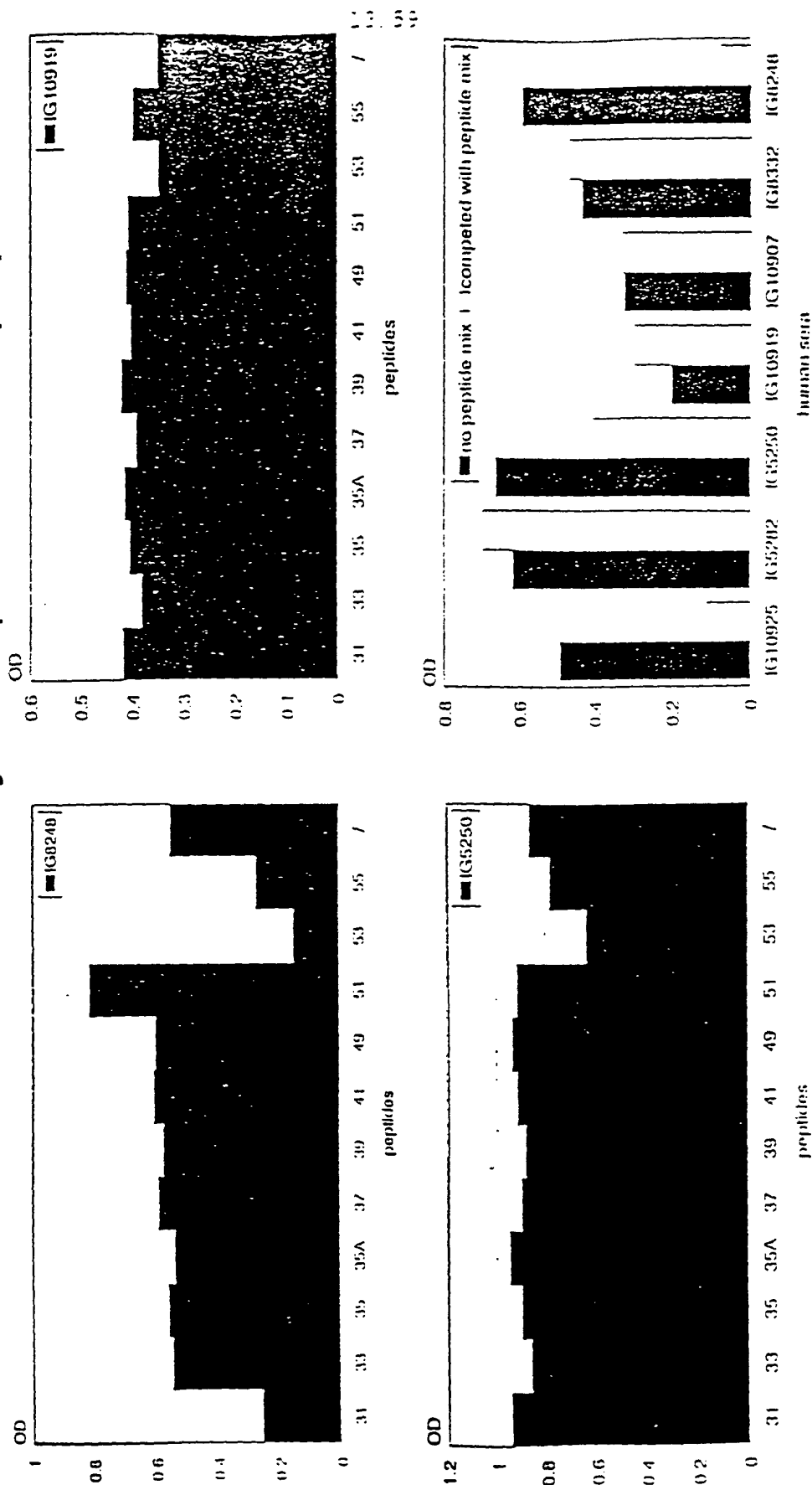
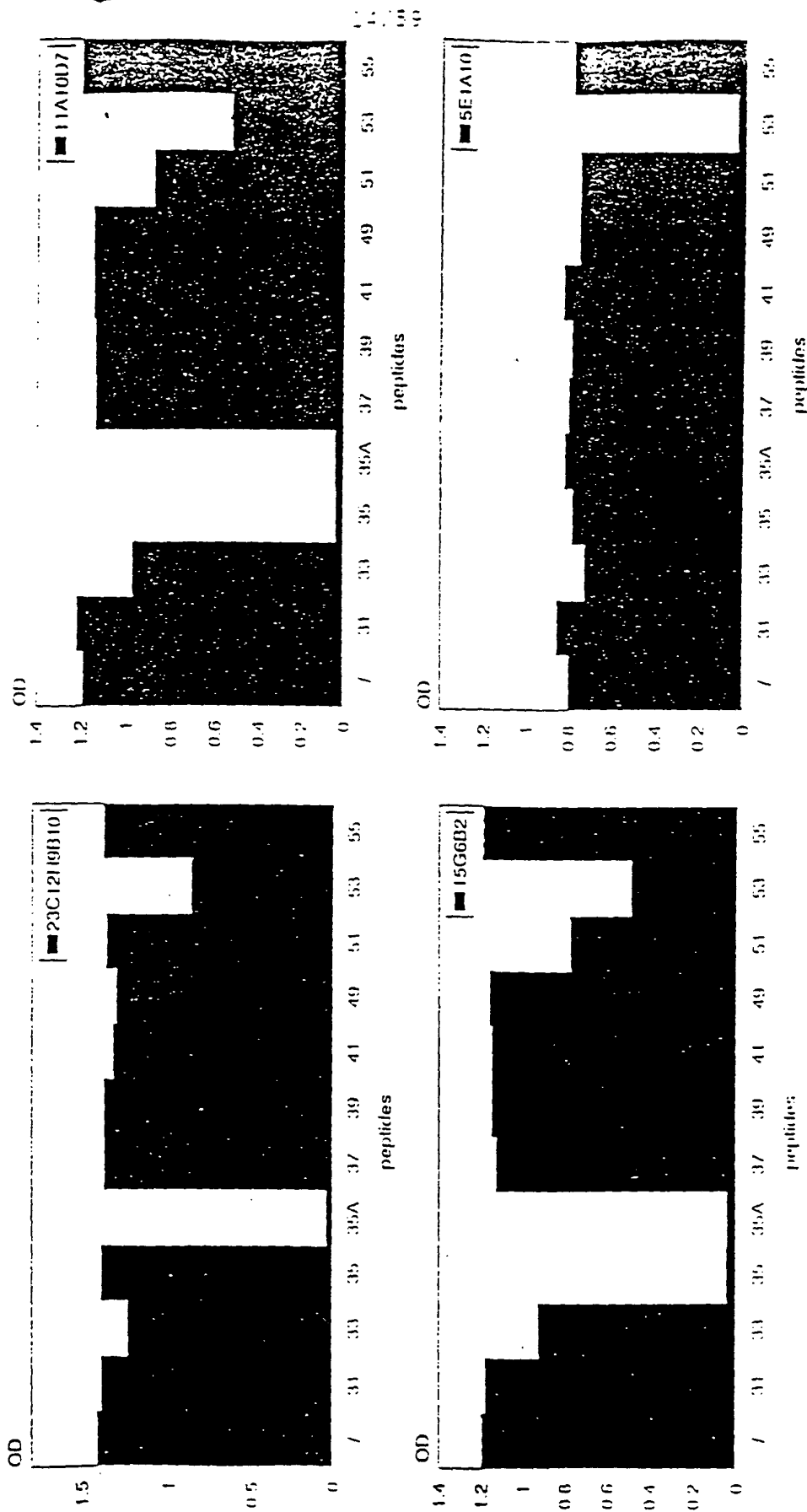


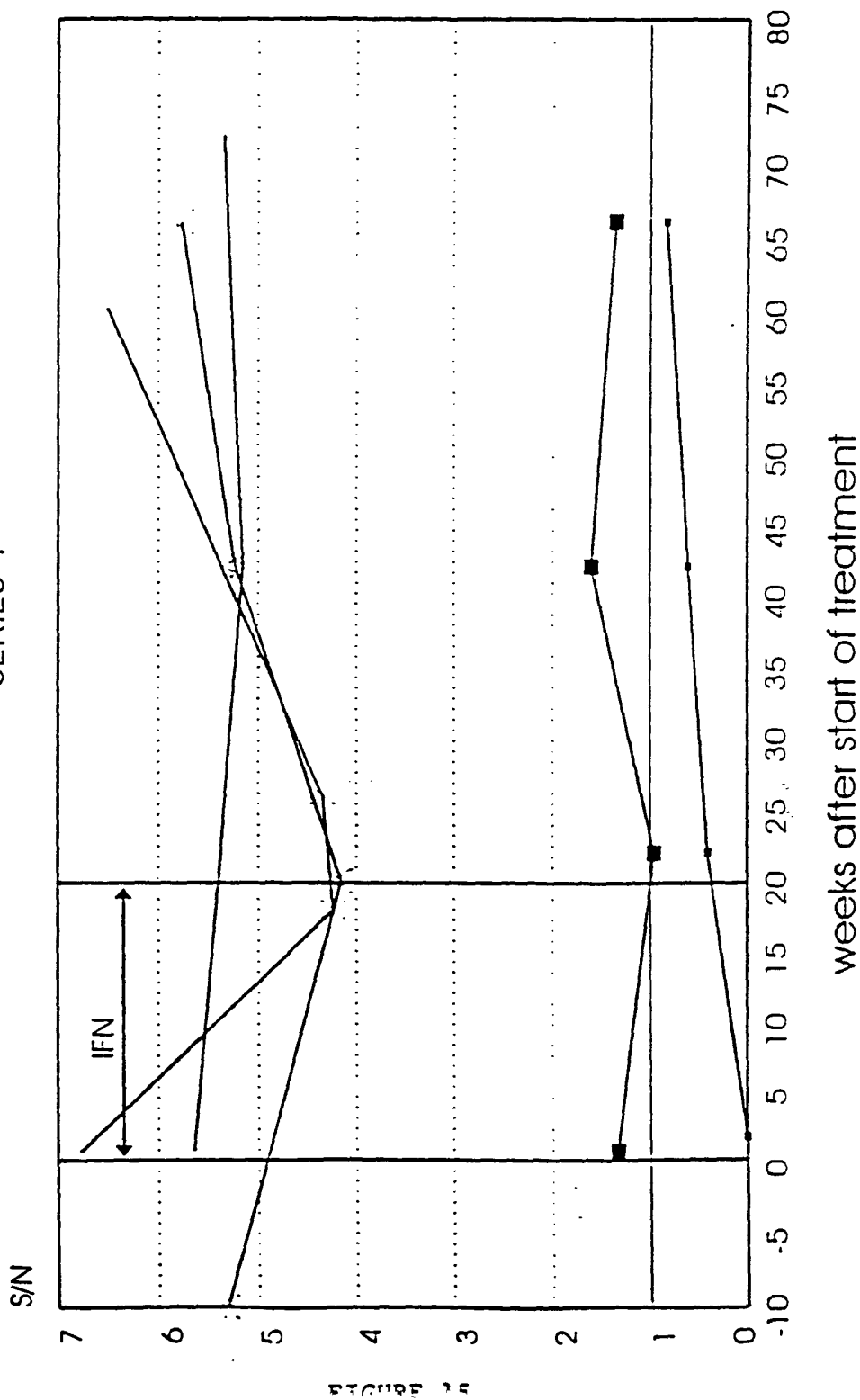
FIGURE 14

Competition of reactivity of anti-E1 Mabs with peptides



Anti-E1 (epitope 1) levels in NON-RESPONDERS to IFN treatment

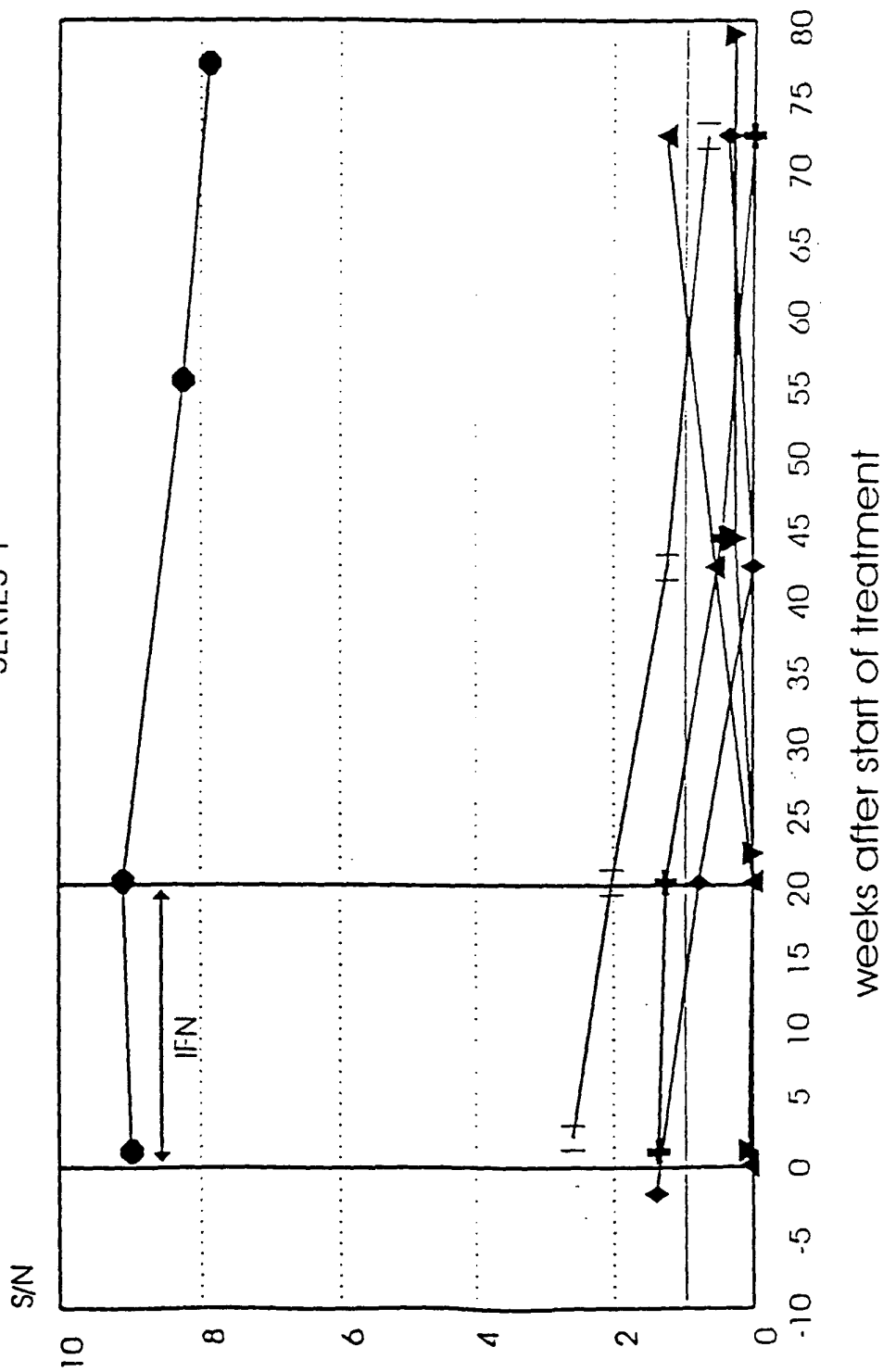
SERIES 1



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Anti-E1 (epitope 1) levels in RESPONDERS to IFN treatment

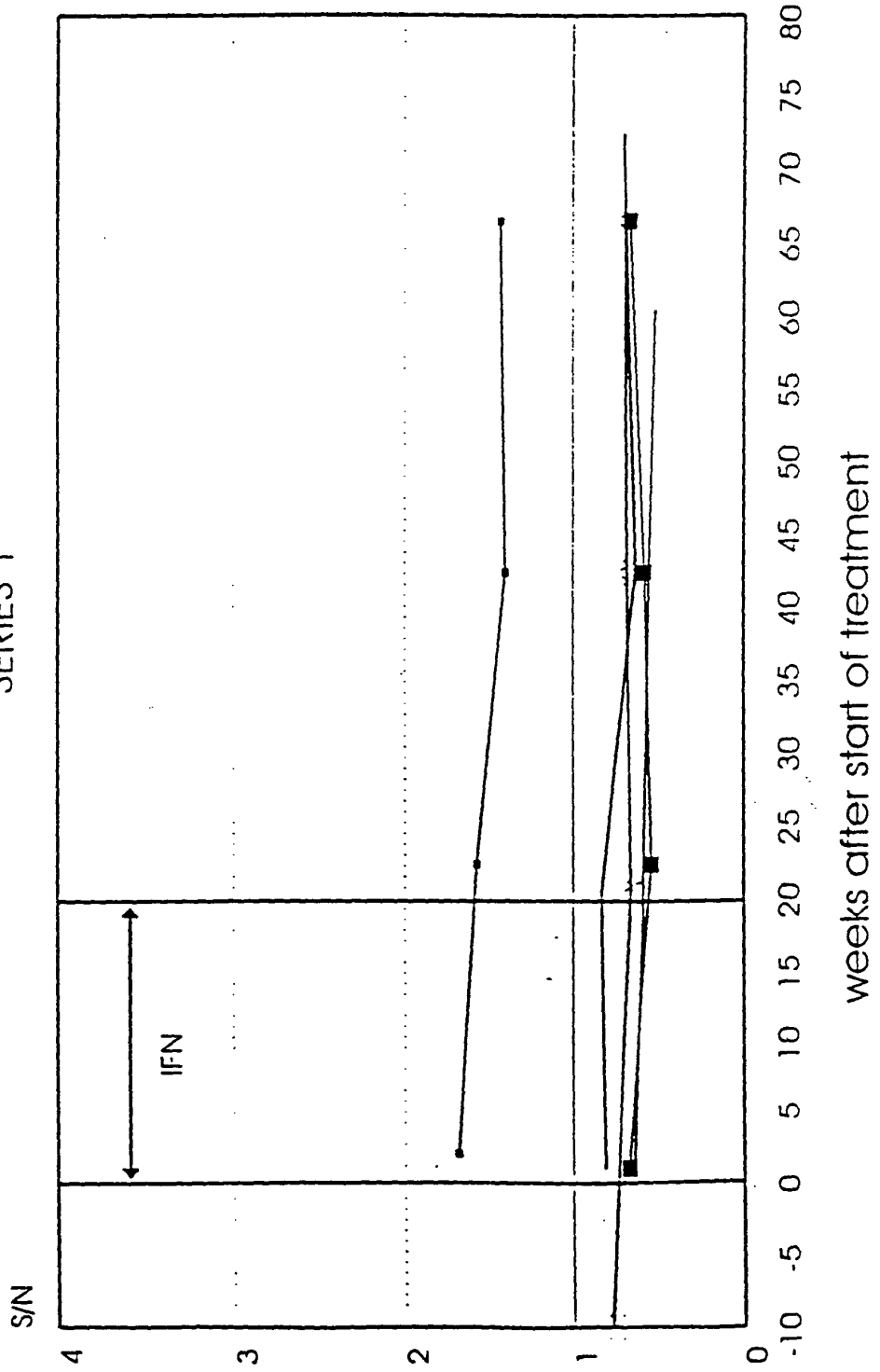
SERIES 1



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ntfi-E1 (epitope 2) levels in NON-RESPONDERS to IFN treatment

SERIES 1



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Anti-E1 (epitope 2) levels in RESPONDERS to IFN treatment

SERIES 1

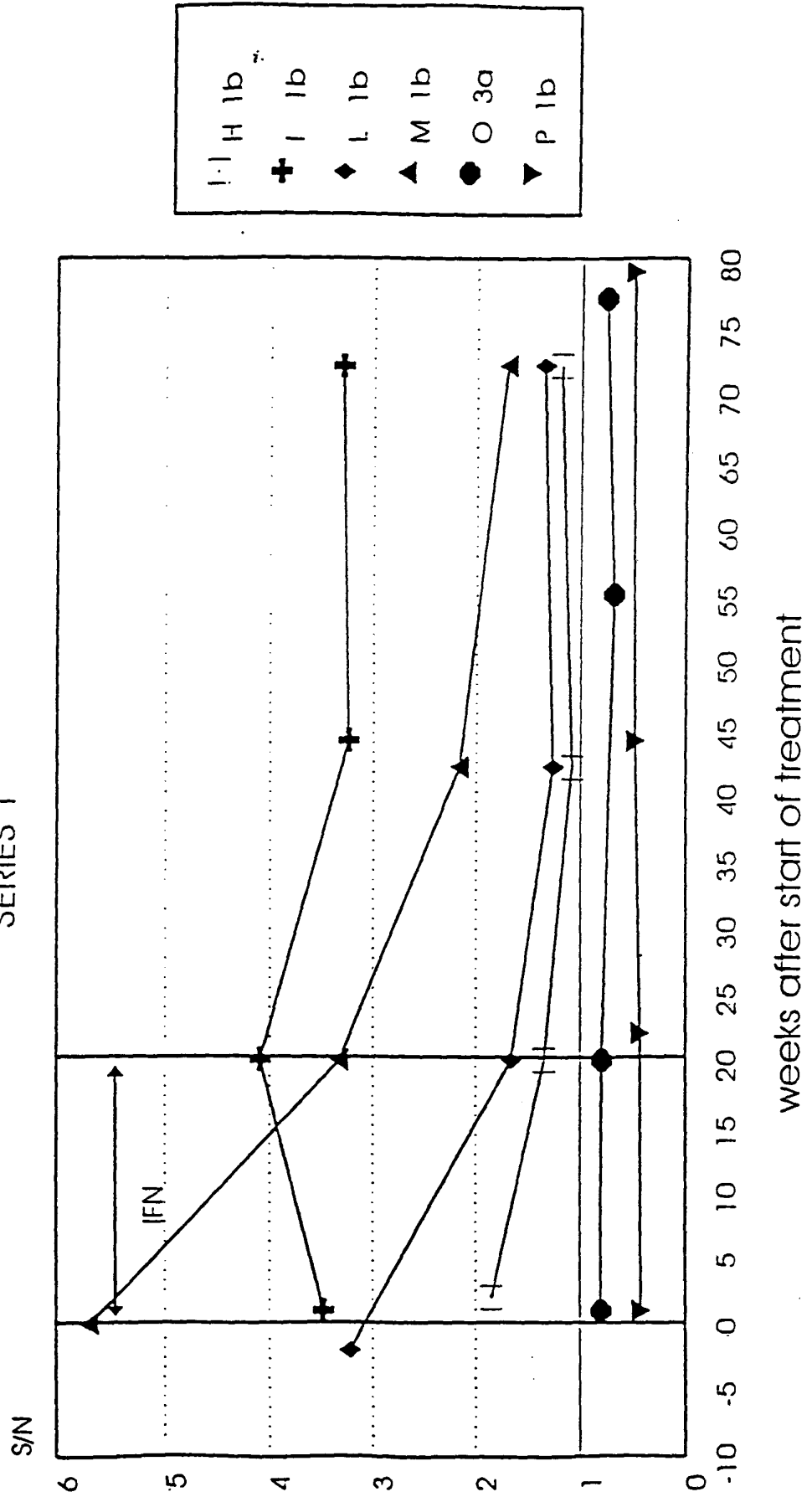


FIGURE 19

Competition of reactivity of anti-E2 Mabs with peptides

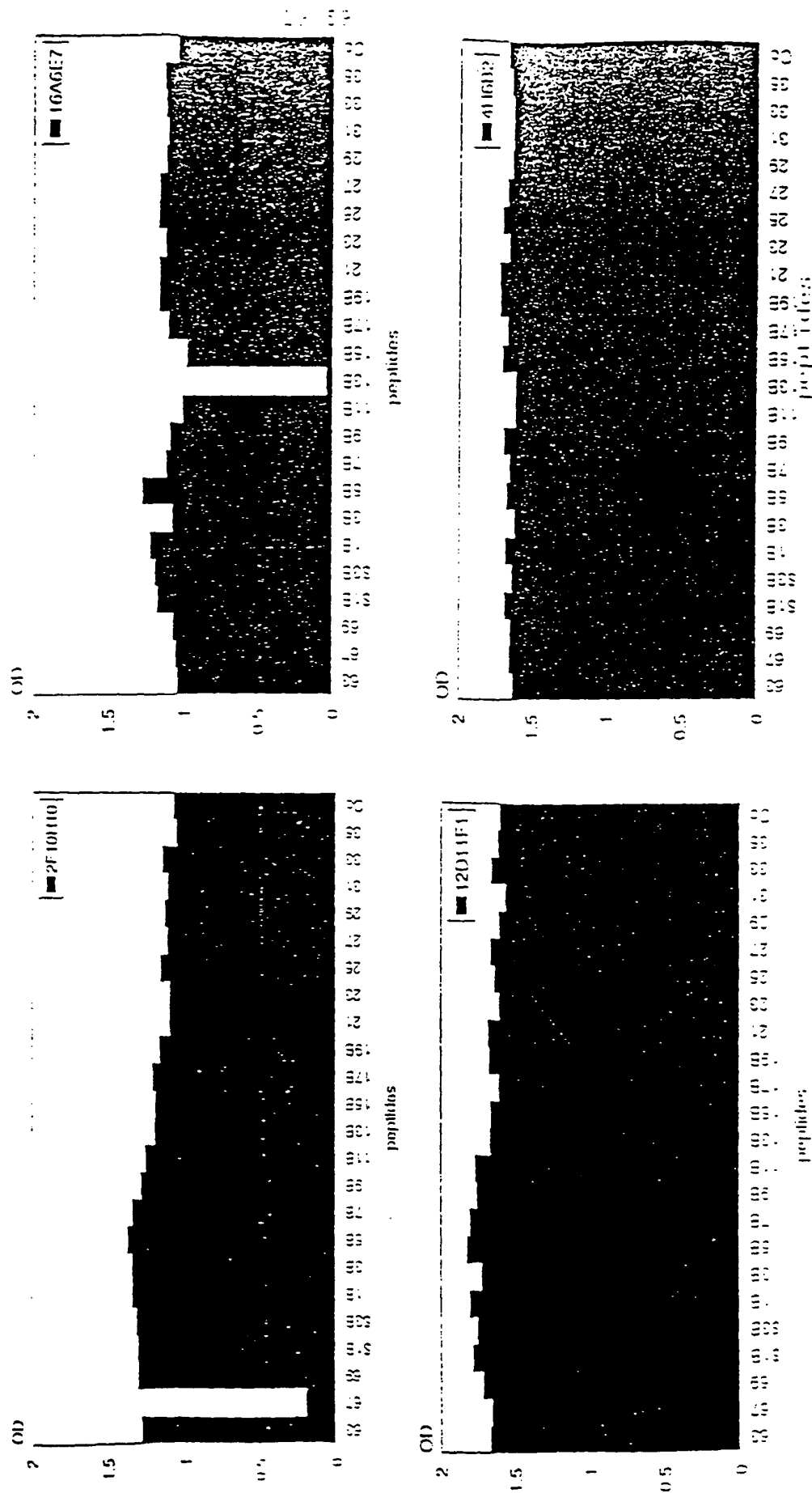
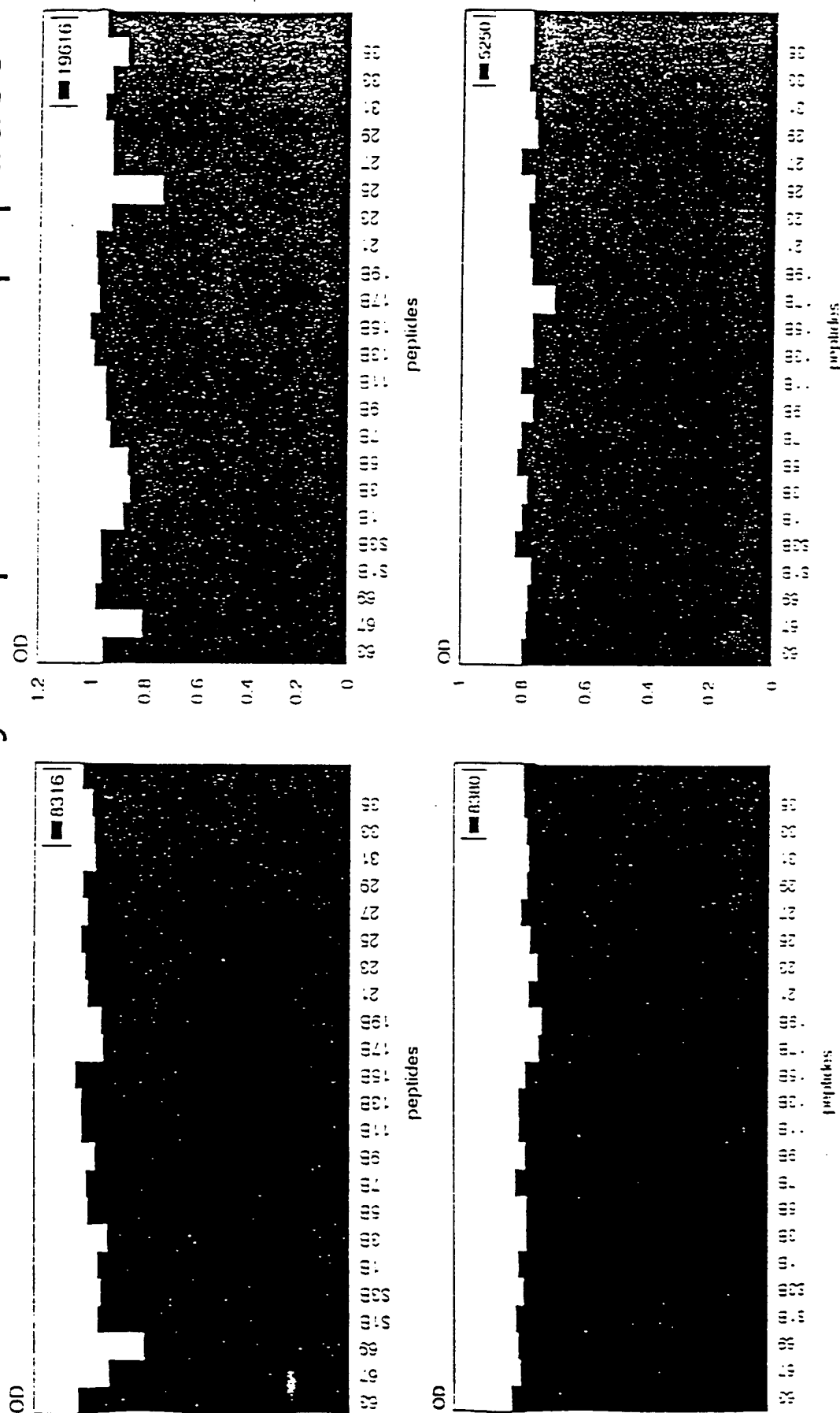


FIGURE 20

Human anti-E2 reactivity competed with peptides



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SEQ ID NO 7 (HCC111A)

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08928757 091297
25150 25280

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SEQ ID NO 16 (HCP52)

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SEQ ID NO 18 (HCP54)

CTATTACCAGTTCATCATCATATCCCA

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08928757.001297

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0922757-091297

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SEQ ID NO 45 (HCCL64)

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452160.452160

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SEQ ID NO 47 (HCCI65)

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CCACATAACGGGTCACCGTATGGCTTGGGATATGATGATGAACTGGTGCCTACAACG
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08926757.094297

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GTATGTCCTGTTGCTCTTCCTTCTCCTGGCAGACGCGCGCATCTGCGCCTGCTTATGGA
TGATGCTGCTGATAGCTCAAGCTGAGGCCGCCTTAGAGAACCTGGTGGTCTCTCAATGC
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SEQ ID NO 49 (HCCI66)

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CCCTGCACTGTCAACTTCACCATCTTCAAGGTTAGGATGTACGTGGGGGGCGTGGAGC
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GCTGCCTGGTACATCAAGGGCAGGCTGGTCCCTGGTGCGGCATACGCCTTCTATGGCG
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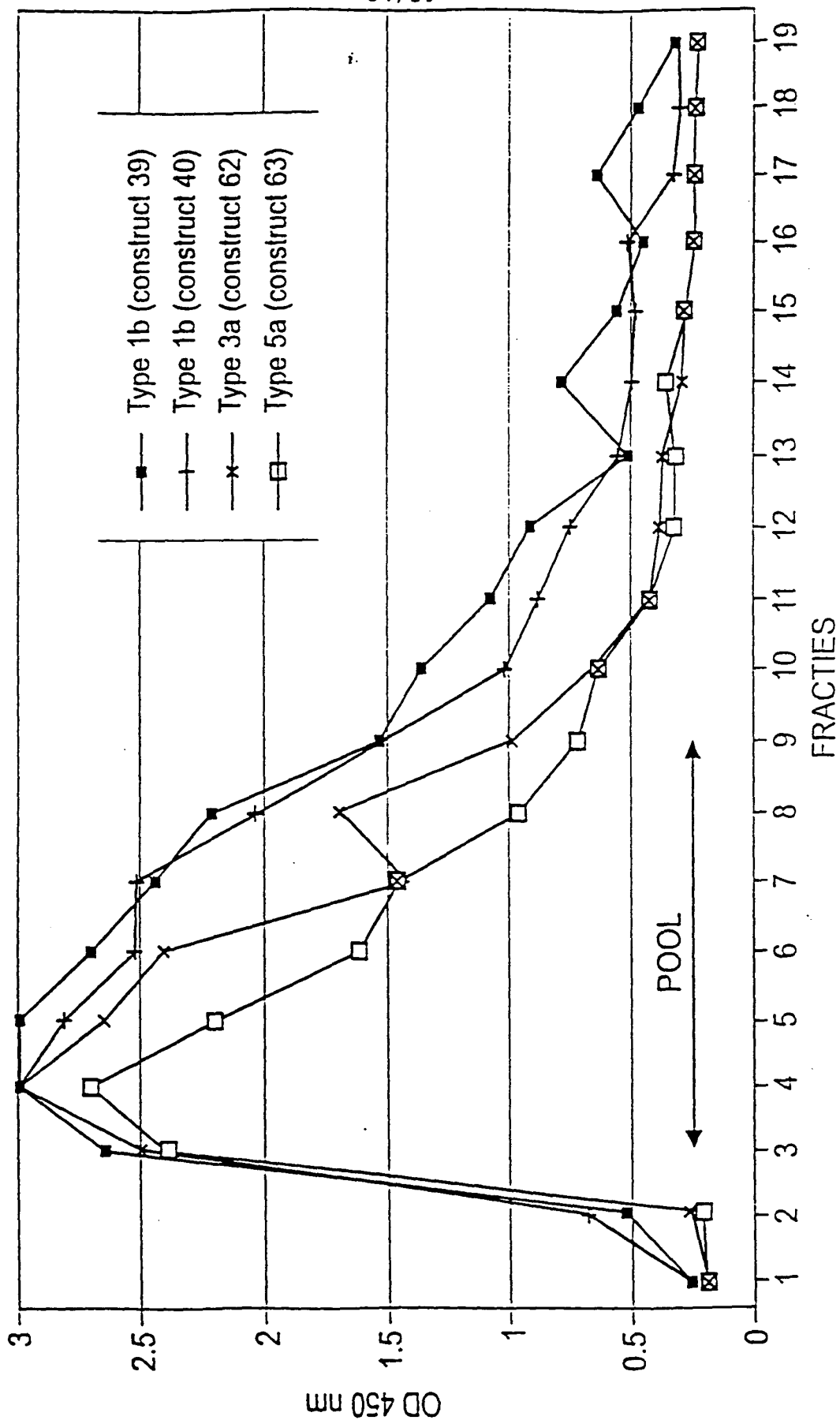
Figure 22

OD measured at 450 nm
construct

Fraction	volume	dilution	39 Type 1b	40 Type 1b	62 Type 5a	63 Type 5a
START	23 ml	1/20	2.517	1.954	1.426	1.142
FLOW THROUGH	23 ml	1/20	0.087	0.083	0.176	0.120
1	0.4 ml	1/200	0.102	0.051	0.048	0.050
2			0.396	0.550	0.090	0.067
3			2.627	2.603	2.481	2.372
4			3	2.967	3	2.694
5			3	2.810	2.640	2.154
6			2.694	2.499	1.359	1.561
7			2.403	2.481	0.347	1.390
8			2.176	1.970	1.624	0.865
9			1.461	1.422	0.887	0.604
10			1.236	0.926	0.543	0.519
11			0.981	0.781	0.294	0.294
12			0.812	0.650	0.249	0.199
13			0.373	0.432	0.239	0.209
14			0.653	0.371	0.145	0.184
15			0.441	0.348	0.151	0.151
16			0.321	0.374	0.098	0.106
17			0.525	0.186	0.099	0.108
18			0.351	0.171	0.083	0.090
19			0.192	0.164	0.084	0.087

252120-252680

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Fraction	volume	dilution	OD measured at 450 nm			
			construct			
			39 Type 1b	40 Type 1b	62 Type 3a	63 Type 5a
20	250 μ l	1/200	0.072	0.130	0.096	0.051
21			0.109	0.293	0.084	0.052
22			0.279	0.249	0.172	0.052
23			0.093	0.151	0.297	0.054
24			0.080	0.266	0.438	0.056
25			0.251	0.100	0.457	0.048
26			3	1.649	0.722	0.066
27			3	3	2.526	0.889
28			3	3	3	2.345
29			3	3	2.849	2.580
30			2.227	1.921	1.424	1.333
31			0.263	0.415	0.356	0.162
32			0.071	0.172	0.154	0.064
33			0.103	0.054	0.096	0.057
34			0.045	0.045	0.044	0.051
35			0.043	0.047	0.045	0.046
36			0.045	0.045	0.049	0.040
37			0.045	0.047	0.046	0.048
38			0.046	0.048	0.047	0.057
39			0.045	0.048	0.050	0.057
40			0.046	0.049	0.048	0.049

0092875 091397
25282680

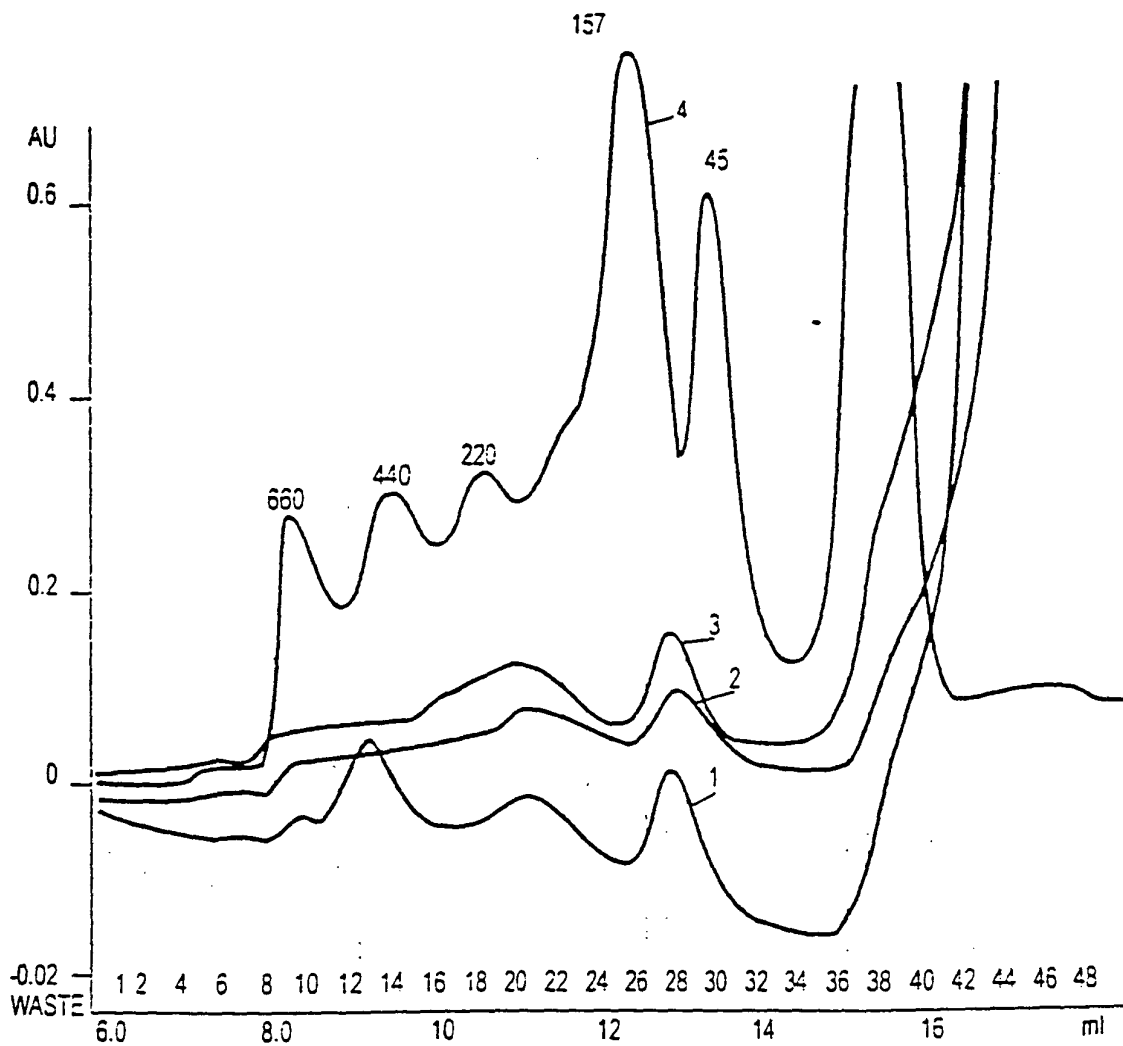


FIGURE 25

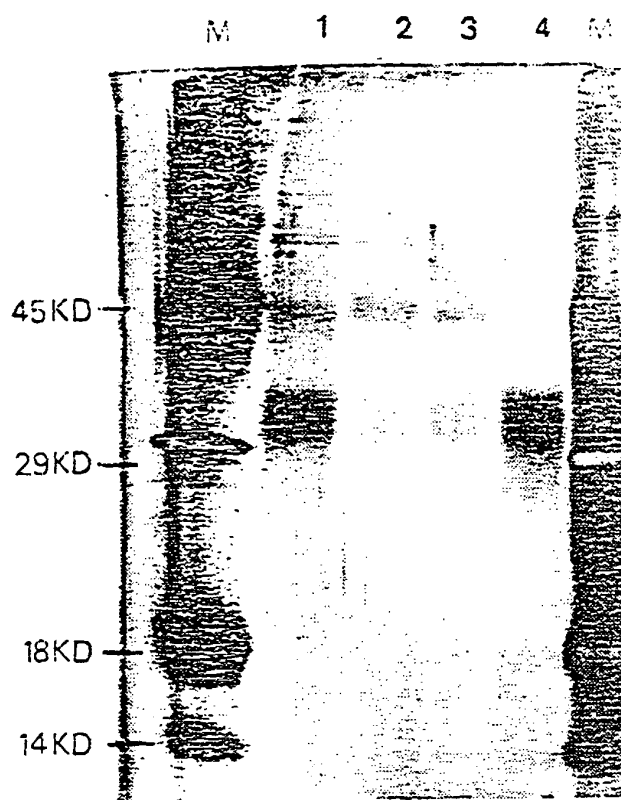


Figure 25

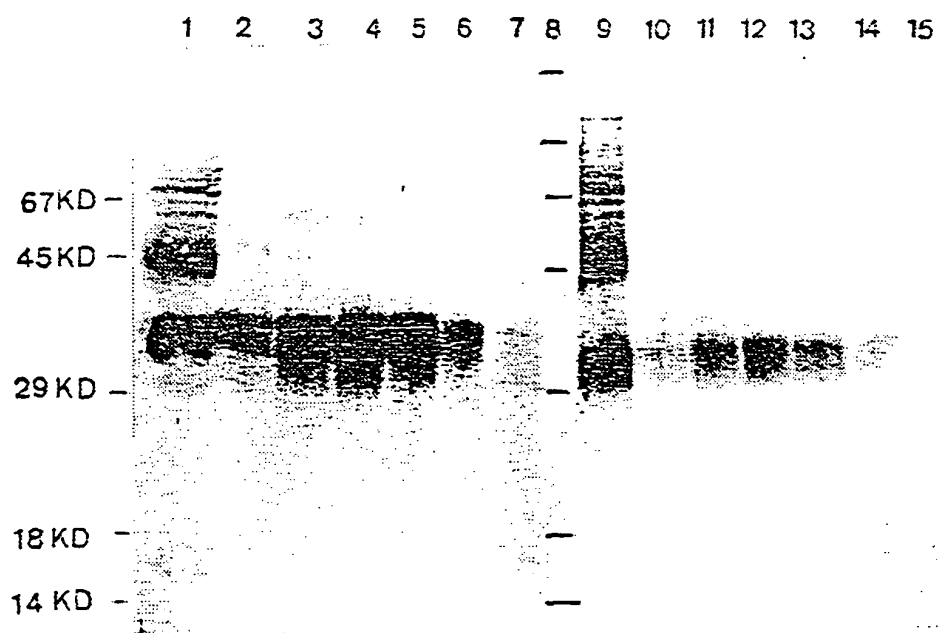


Figure 27

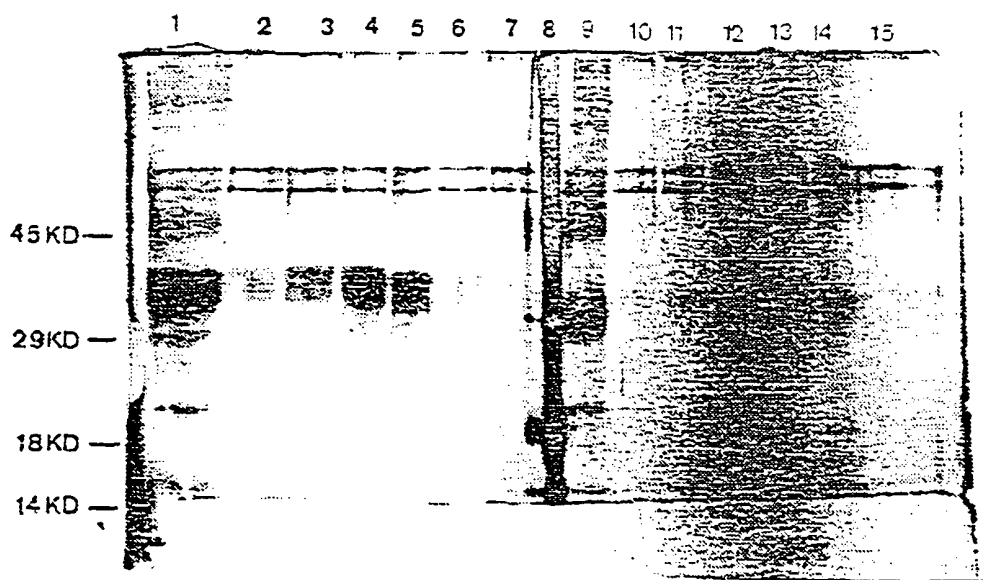


Figure 28

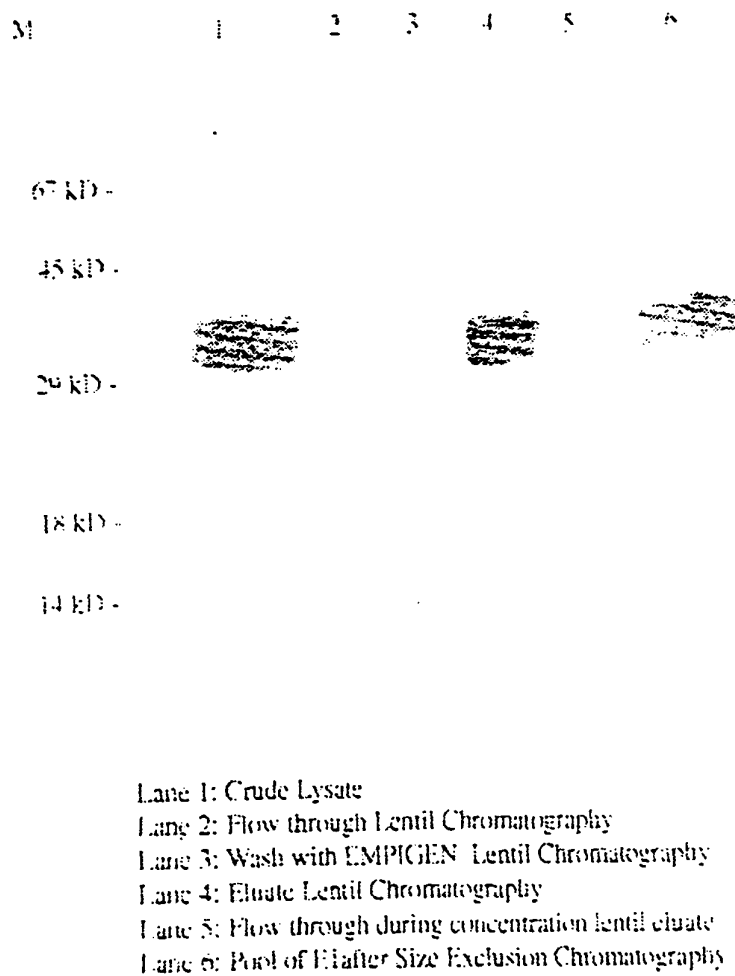


Figure 29: Western Blot Analysis with anti-E1 mouse monoclonal 5E1A10

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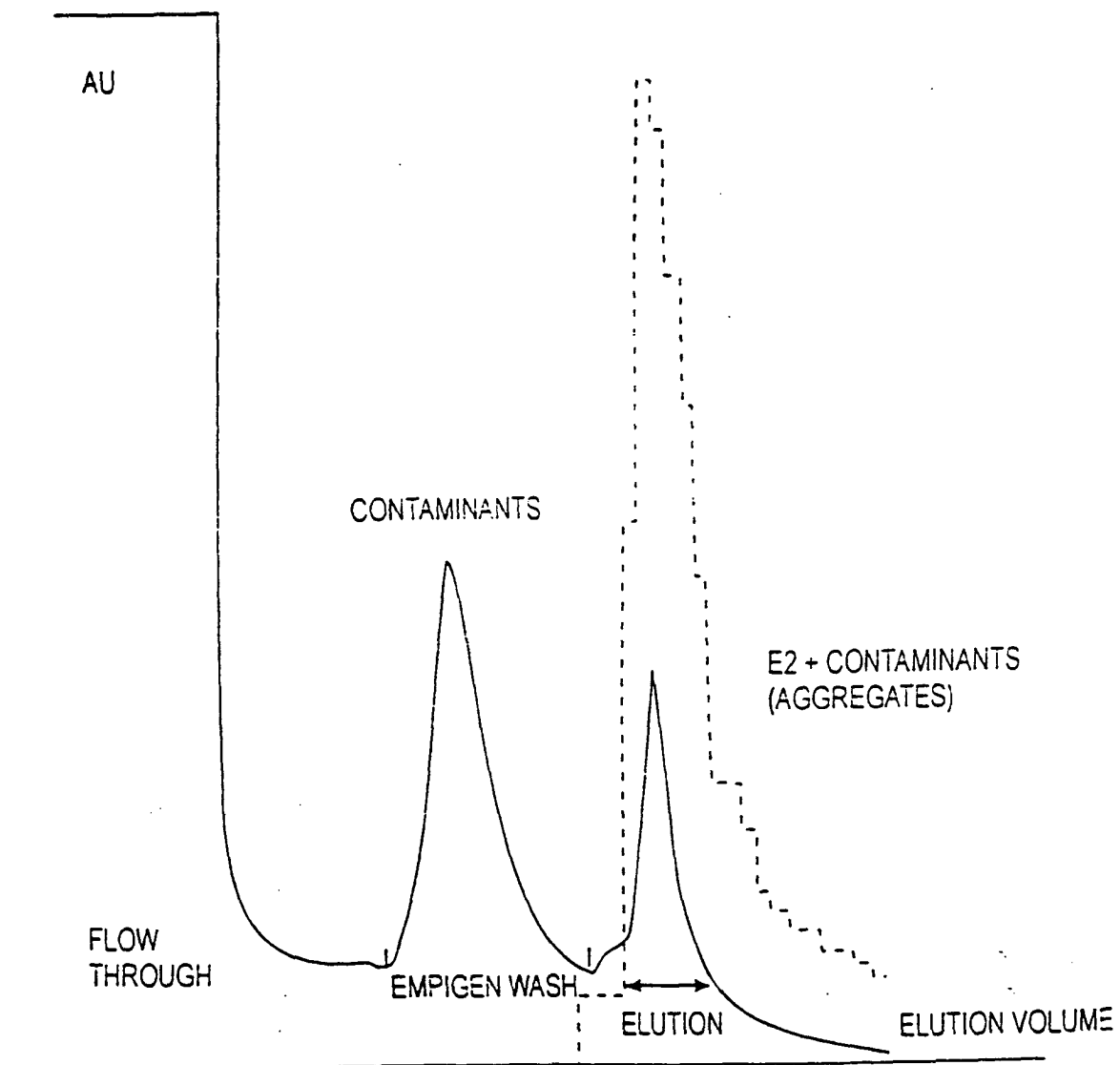
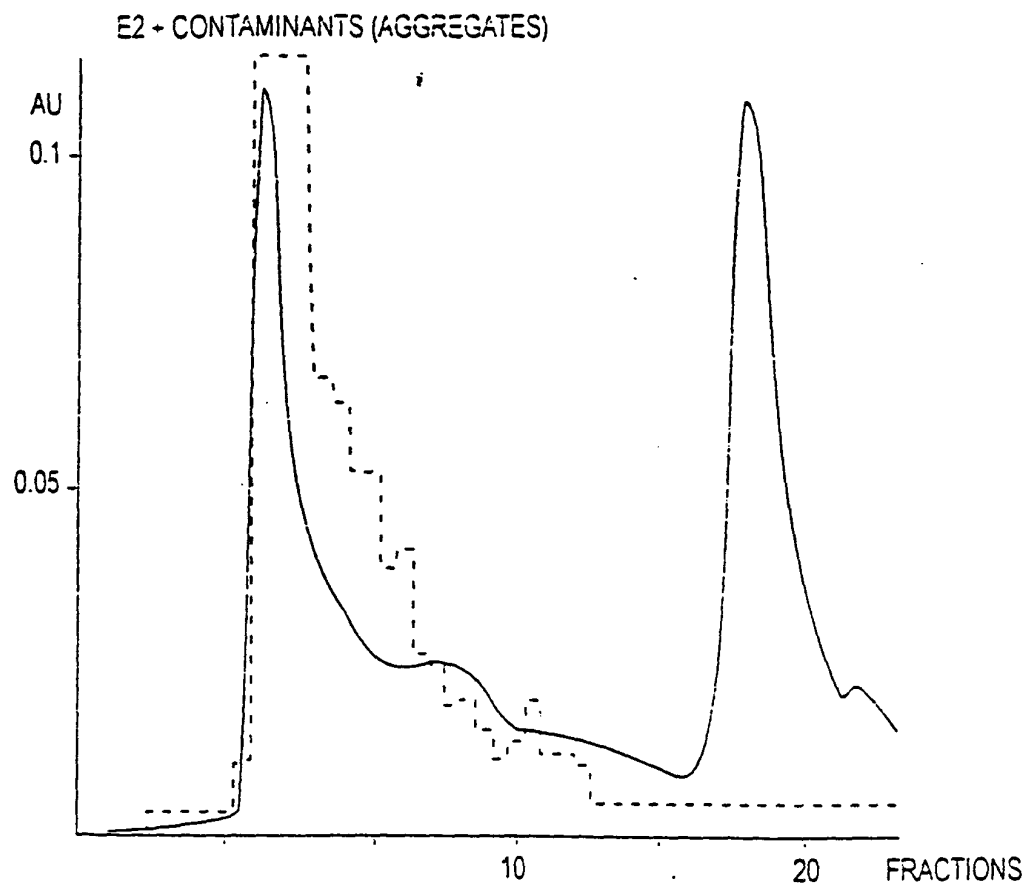


FIGURE 30

A: NON - REDUCED



B: REDUCED

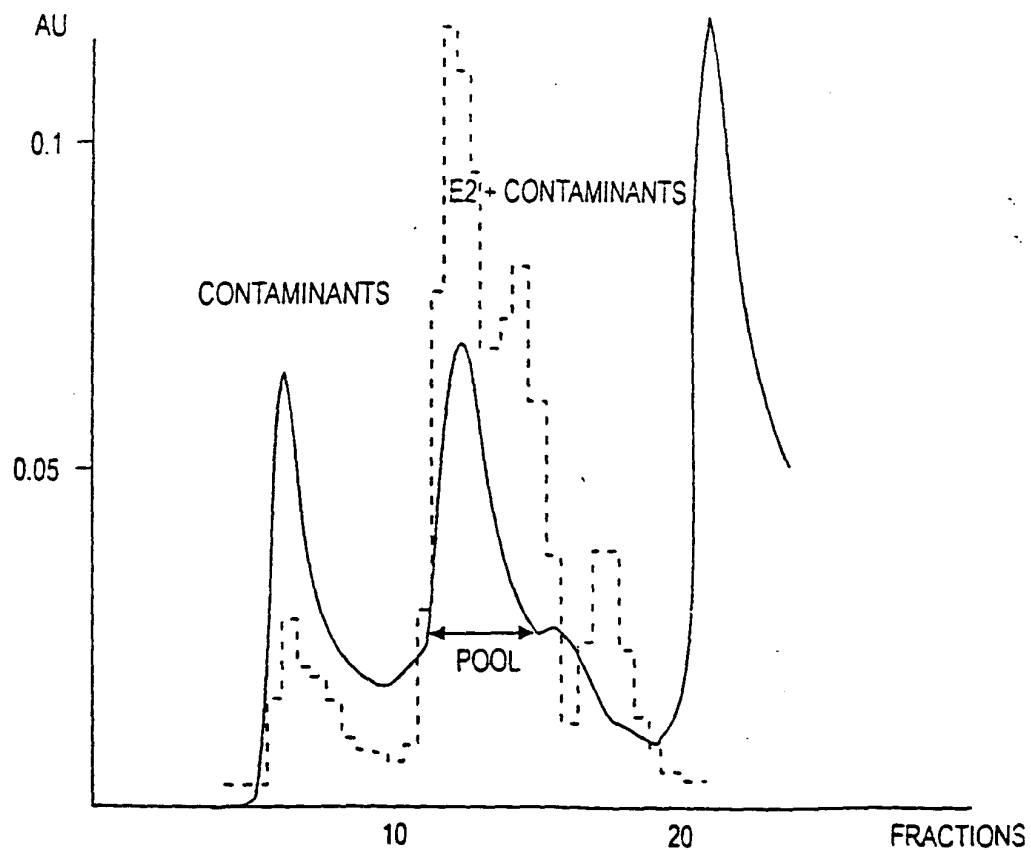


FIGURE 21

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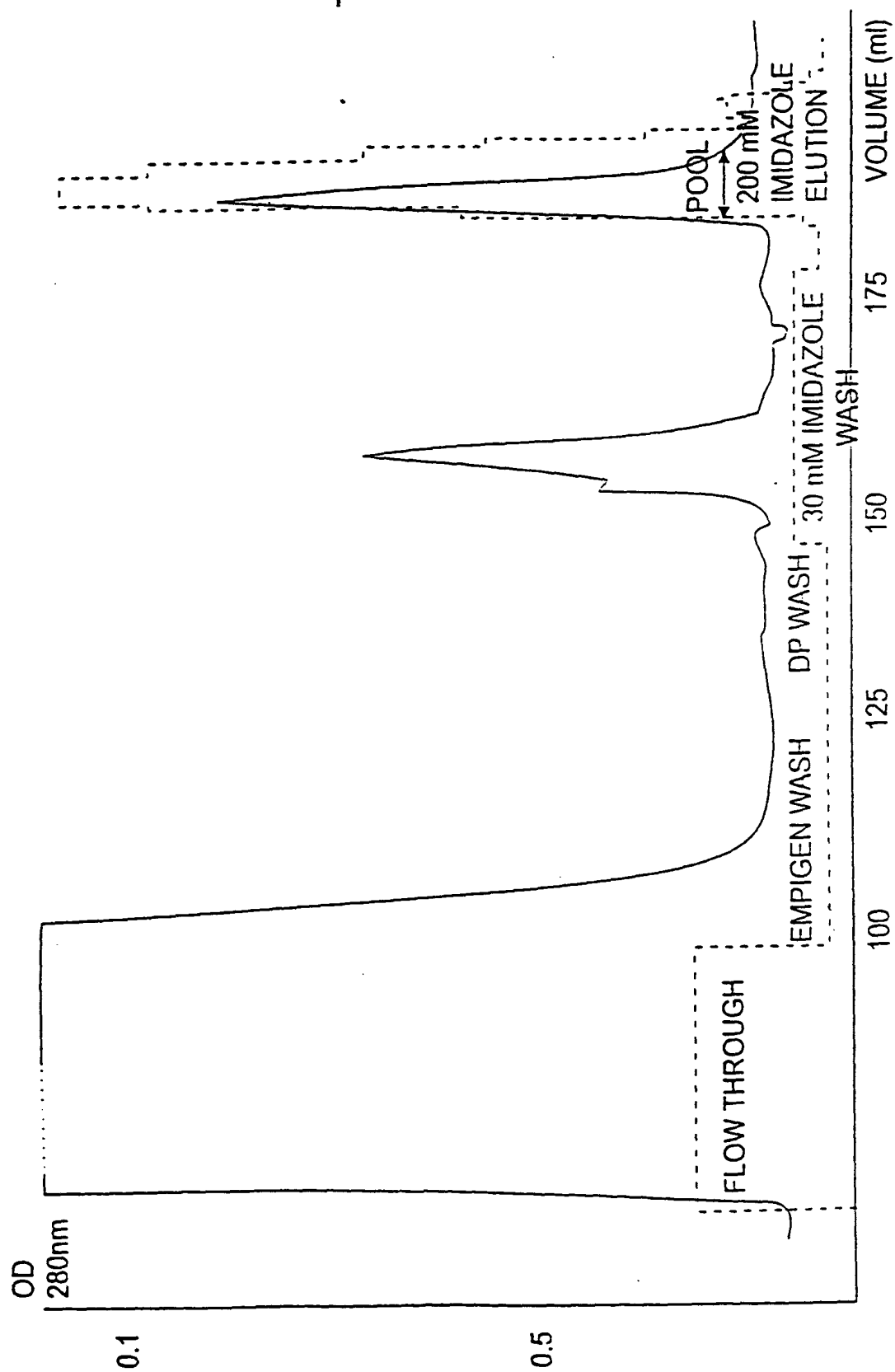
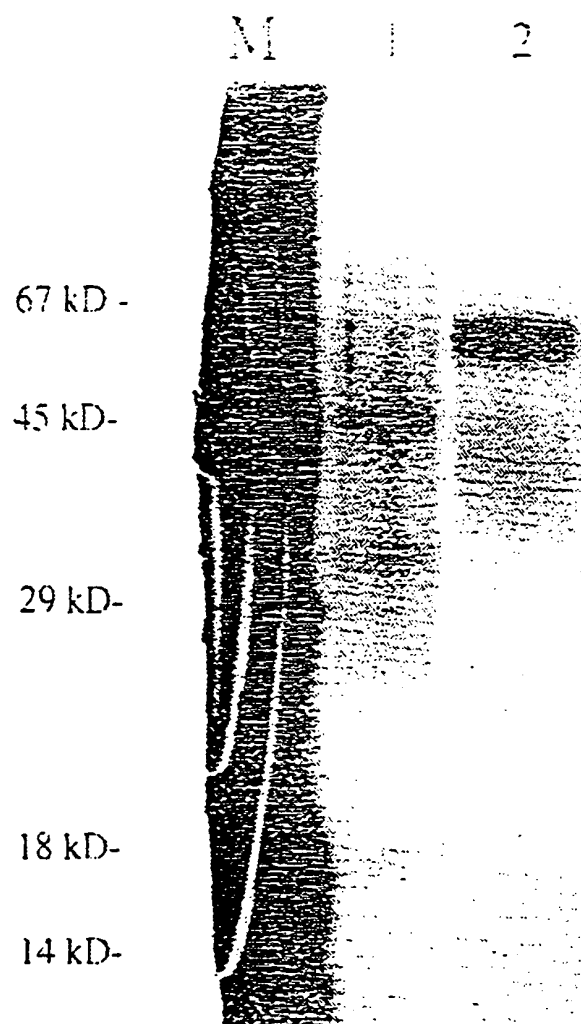


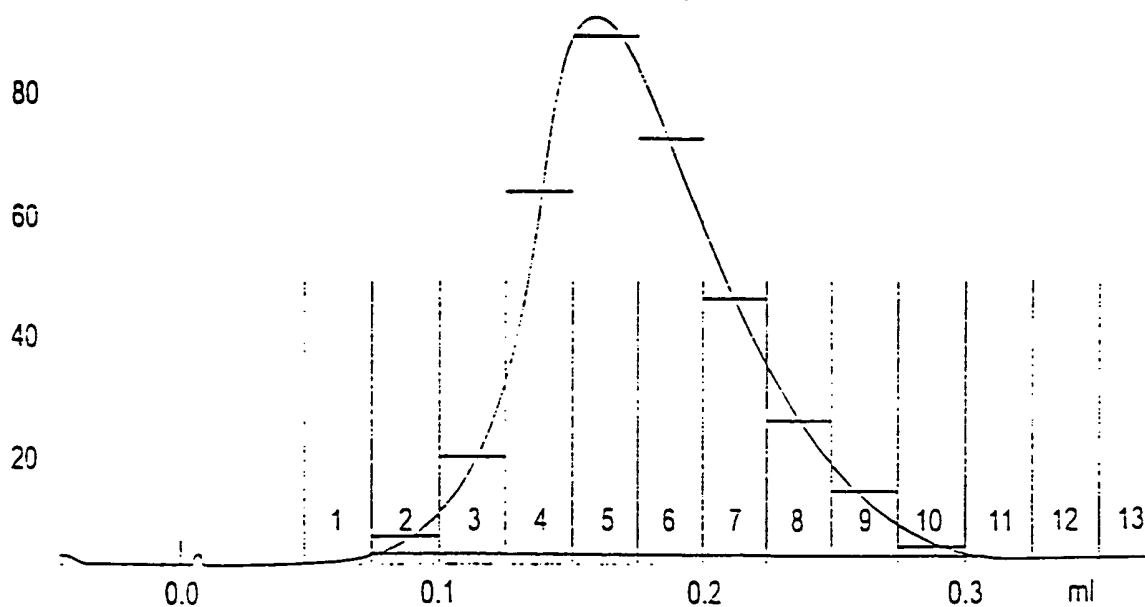
FIGURE 32

FIGURE 33:
SILVER STAIN OF PURIFIED E2



1. 30 mM IMIDAZOLE WASH Ni-IMAC
2. 0.5 μ g E2

45 59 Figure 34



No.	Ret. (ml)	Peak start (ml)	Peak end (ml)	Dur (ml)	Area (ml*mAU)	Height (mAU)
1	-0.45	-0.46	-0.43	0.04	0.0976	4.579
2	1.55	0.75	3.26	2.51	796.4167	889.377
3	3.27	3.26	3.31	0.05	0.0067	0.224
4	3.33	3.32	3.33	0.02	0.0002	0.018

Total number of detected peaks = 4

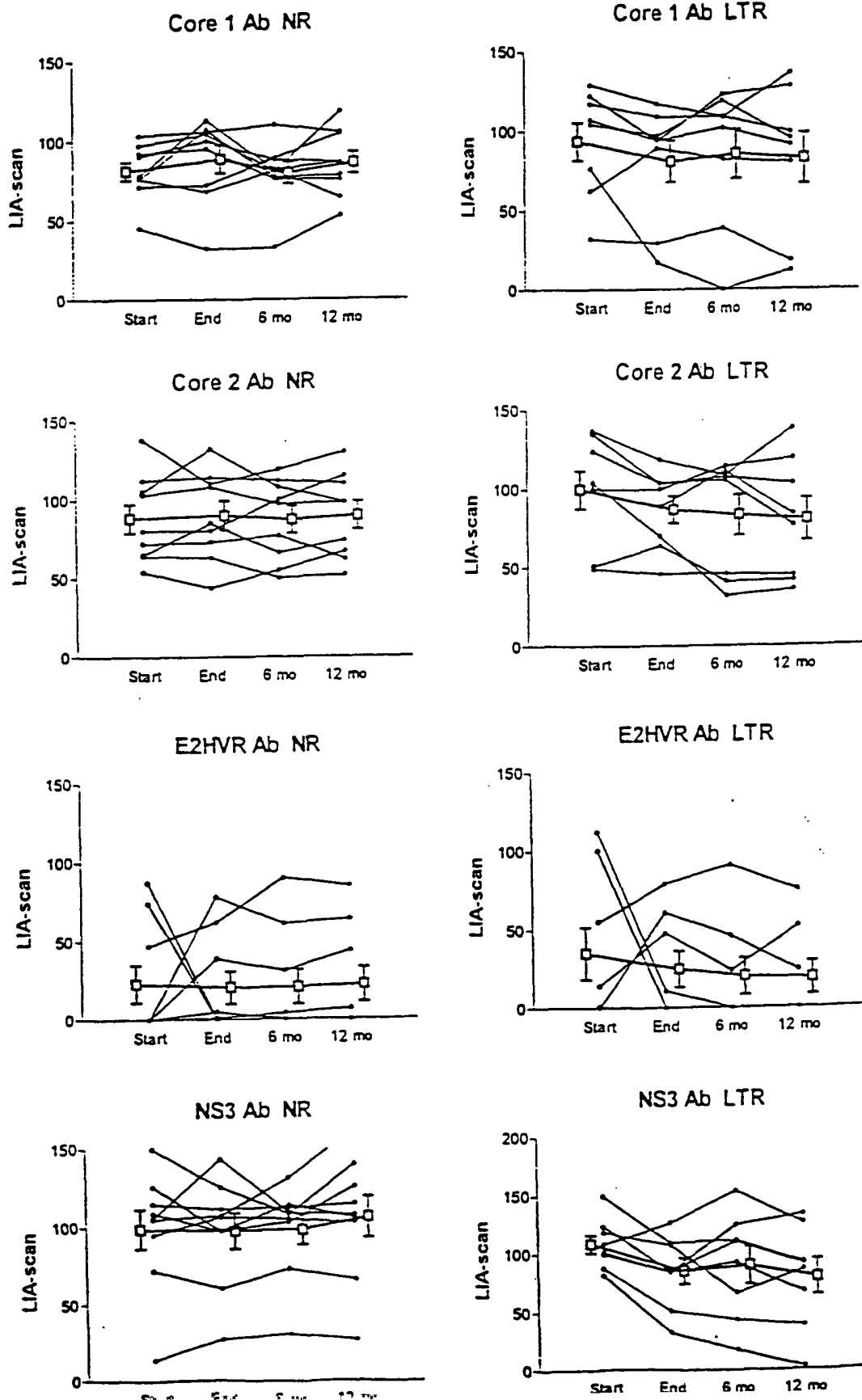
Total Area above baseline = 0.796522 ml*mAU

Total area in evaluated peaks = 0.796521 ml*mAU

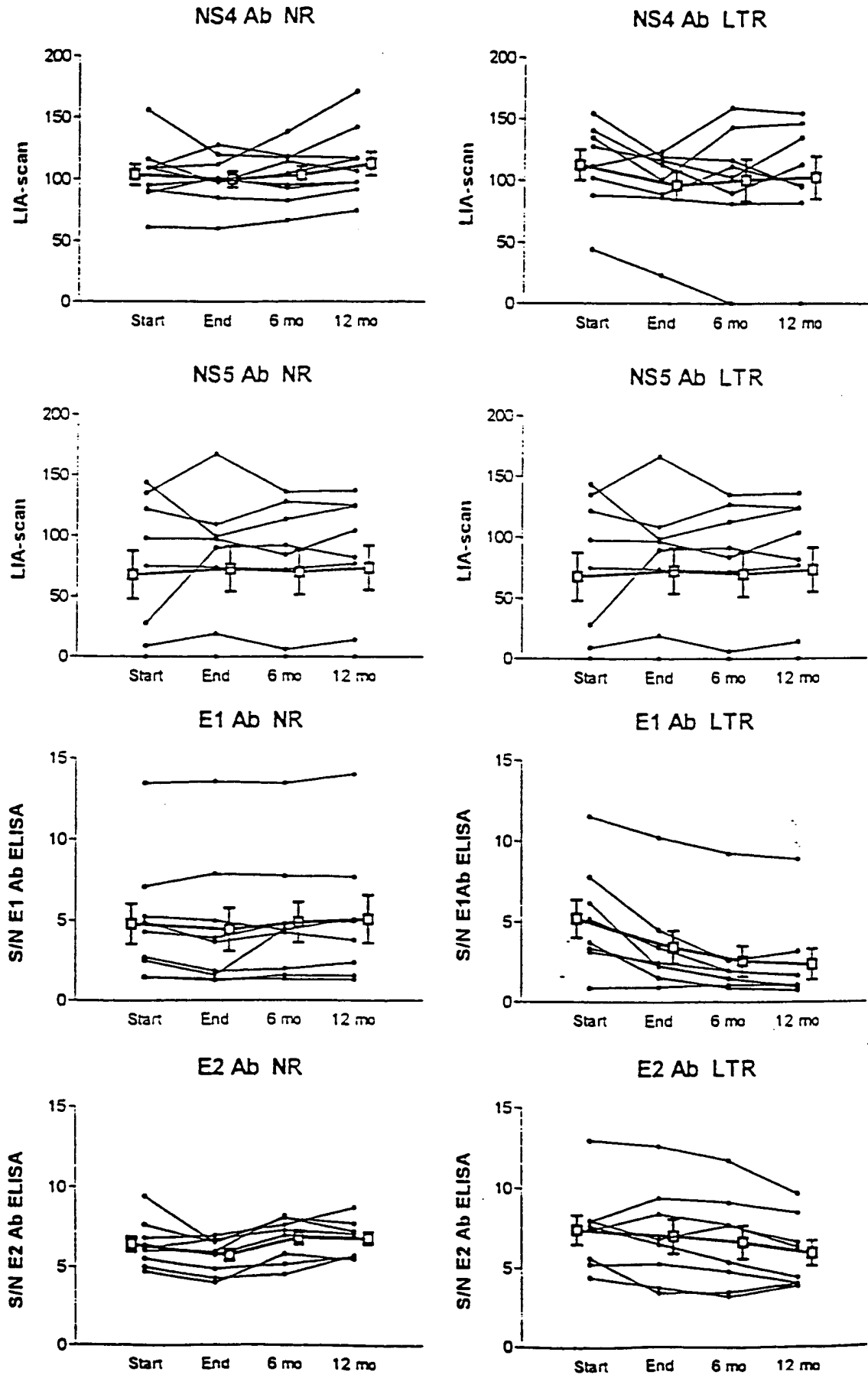
Ratio peak area / total area = 0.999999

Total peak duration = 2.613583 ml

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FIGURE 35A

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FIGURE 35B

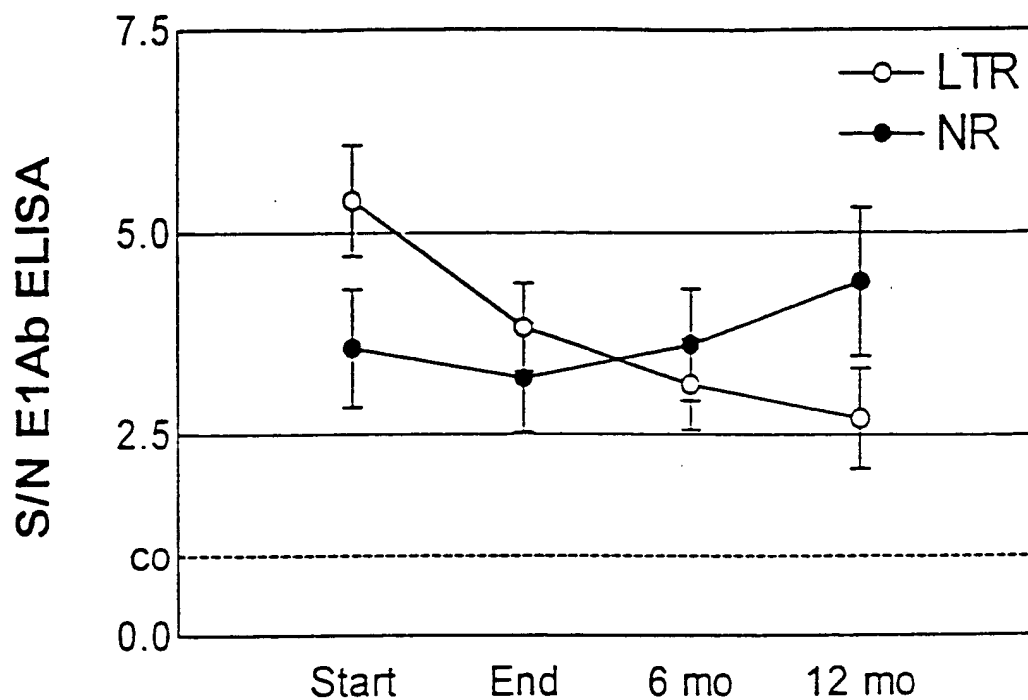
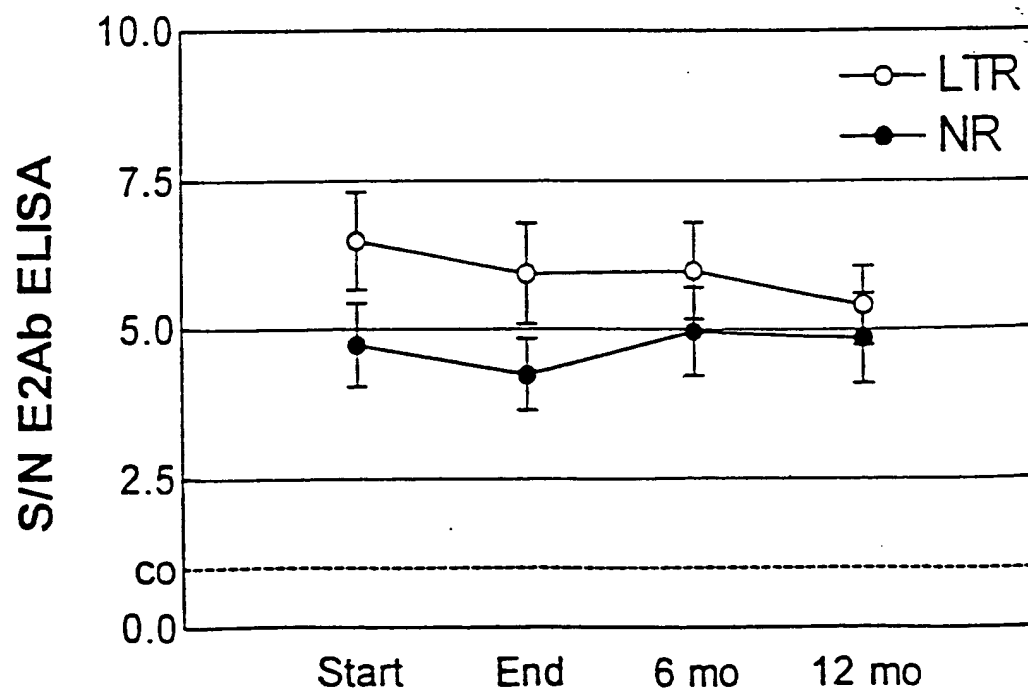
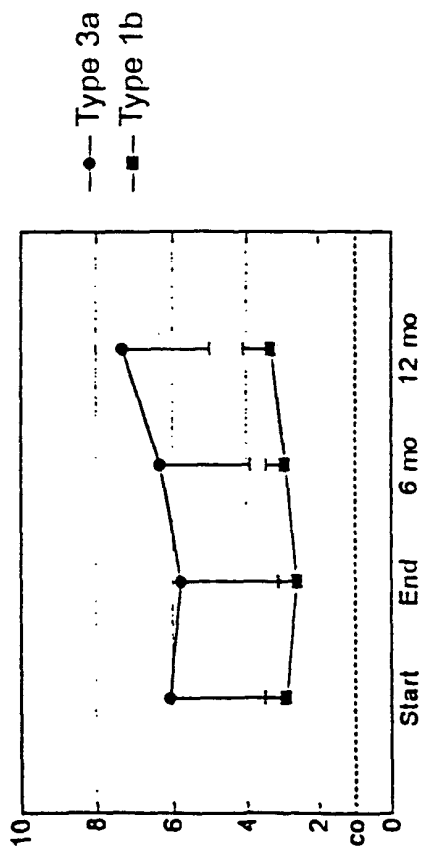
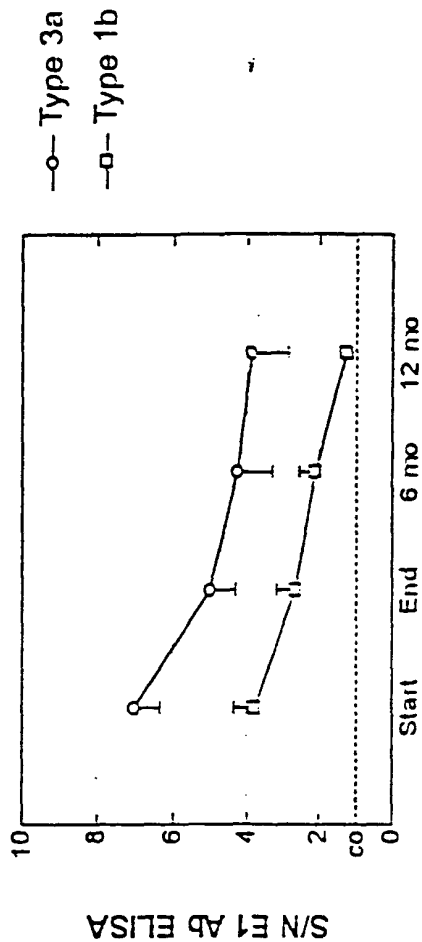
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Figure 36**E1 Ab****E2 Ab**

FIGURE 37

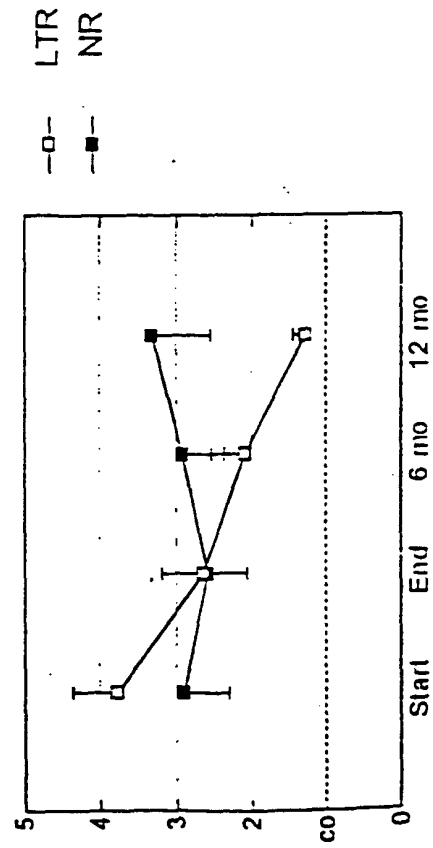
Non Responders



Long Term Responders



Type 1b



Type 3a

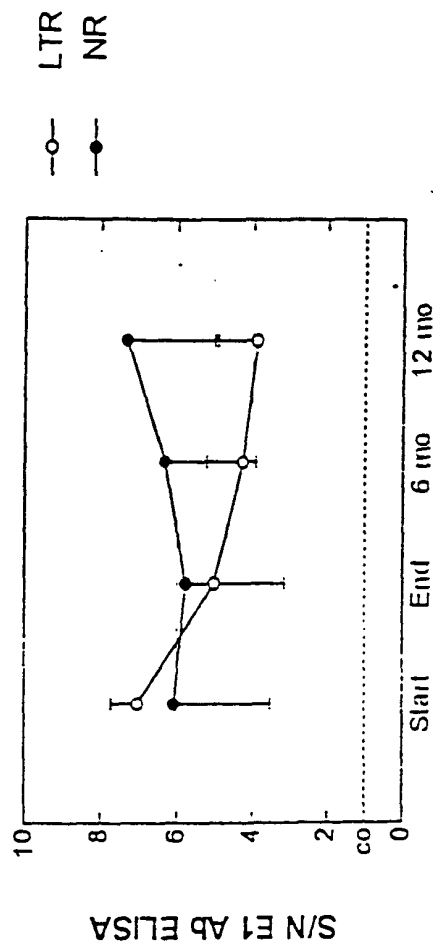
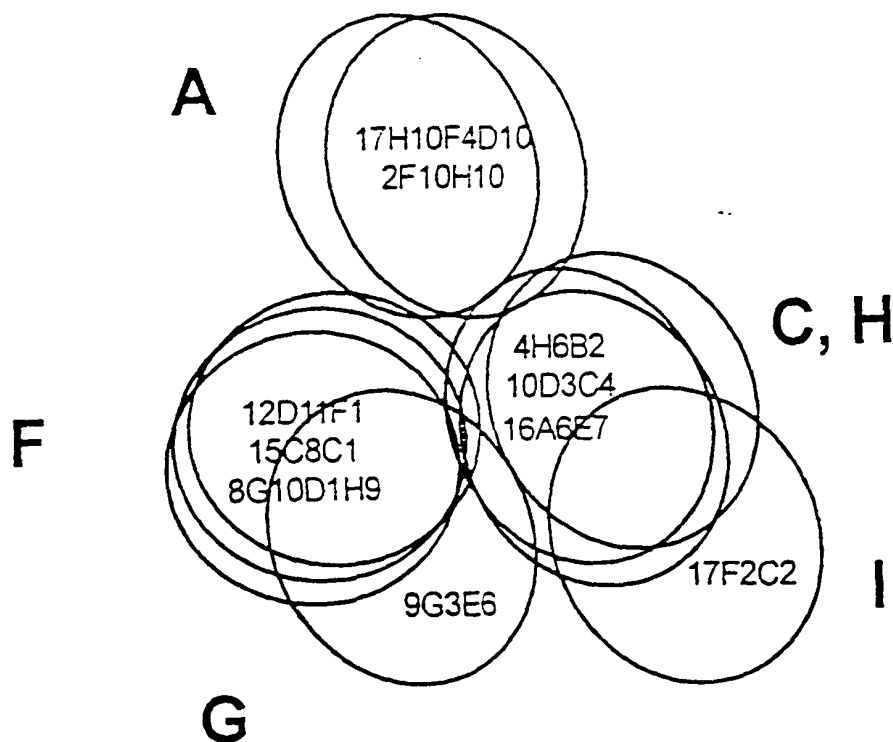


Figure 38

Relative Map Positions of
anti-E2 monoclonal antibodies



252500 252500

PARTIAL DEGLYCOSYLATION OF HCV E1 ENVELOPE PROTEIN

Endoglycosidase H (Endo H) Glycopeptidase F (PNGase F)

0µg 0.6µg 6µg 60µg 0.6µg 6µg 0.4µg 4µg 40µg 400µg

106.0
80.0
49.5
32.5
27.5
18.5

6
5
4
3
2
1
0

Figure 39

PARTIAL TREATMENT OF HCV E2/E2s ENVELOPE PROTEINS BY PNGase F

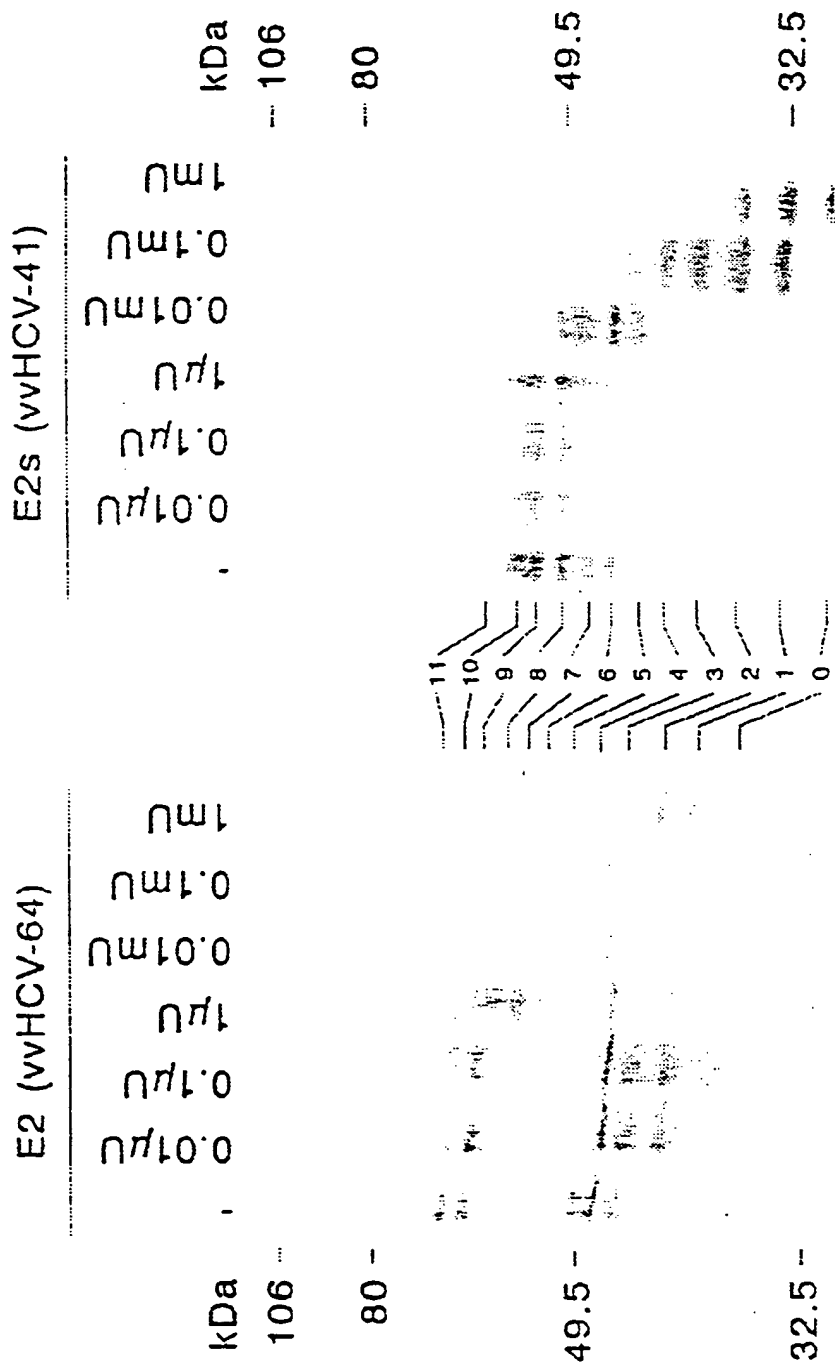


Figure 40

In Vitro Mutagenesis of HCV E1 glycoprotein

Fig. 41

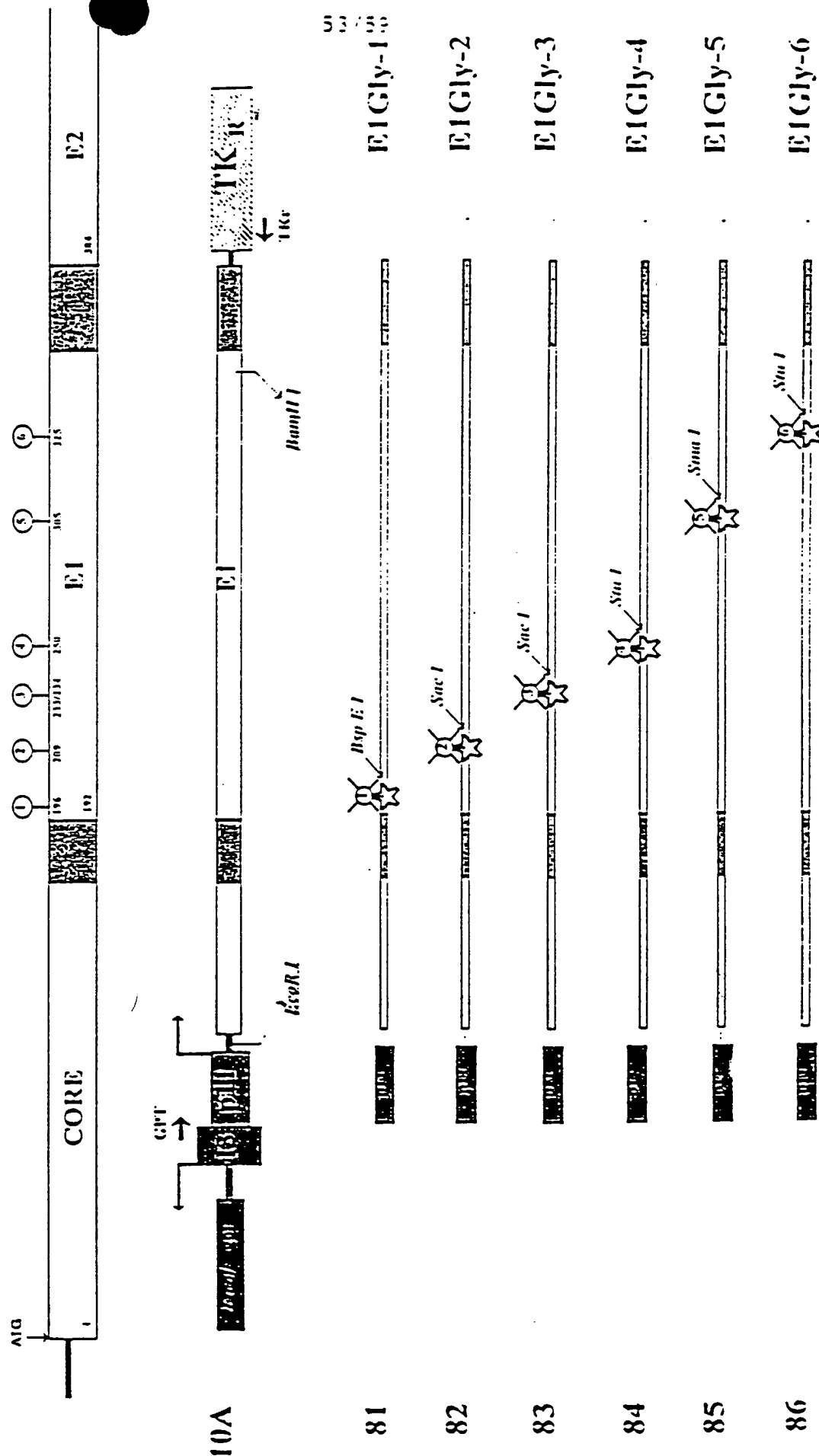


Fig. 42A *In Vitro* Mutagenesis of HCV E1 glycoprotein

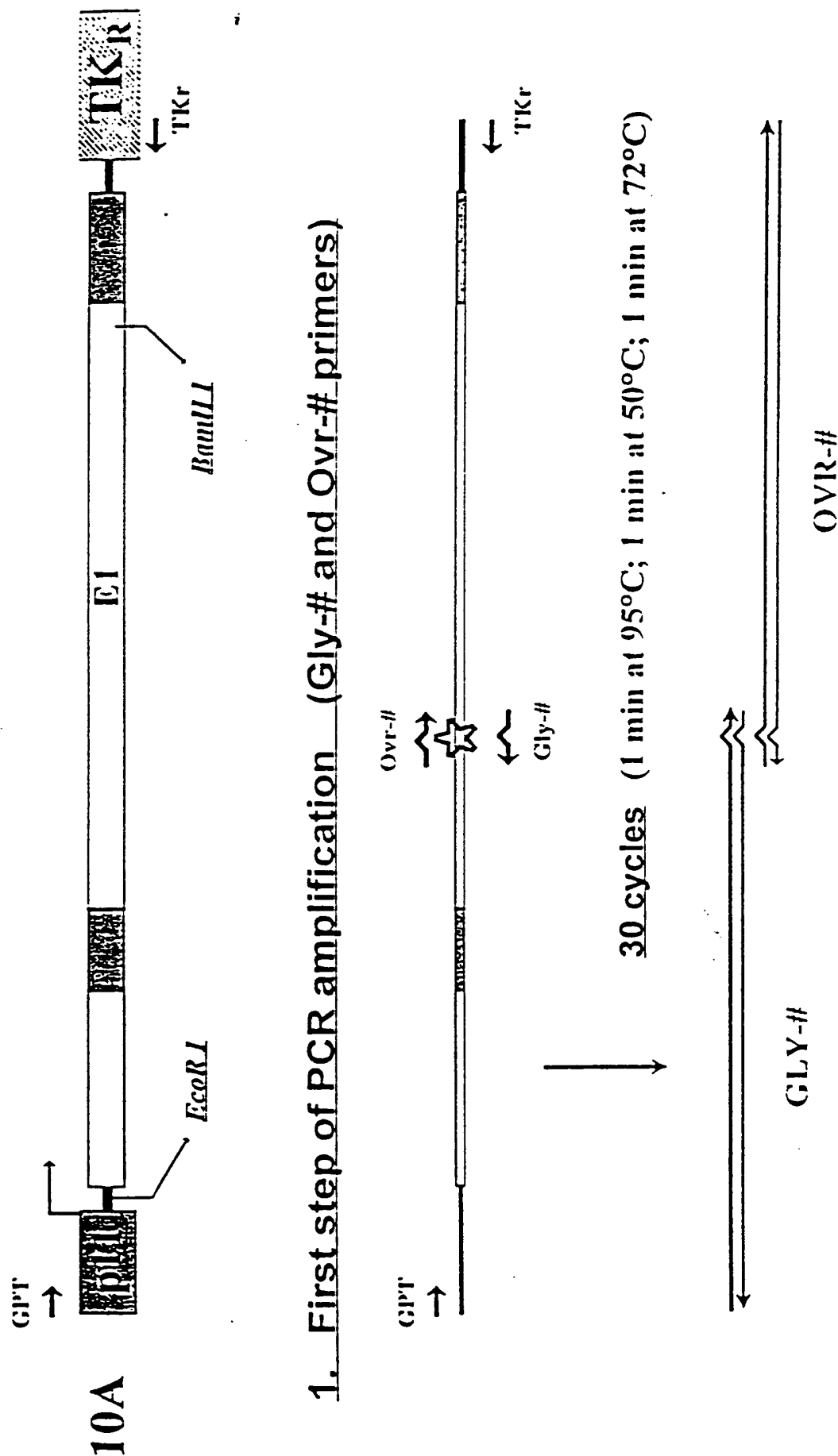
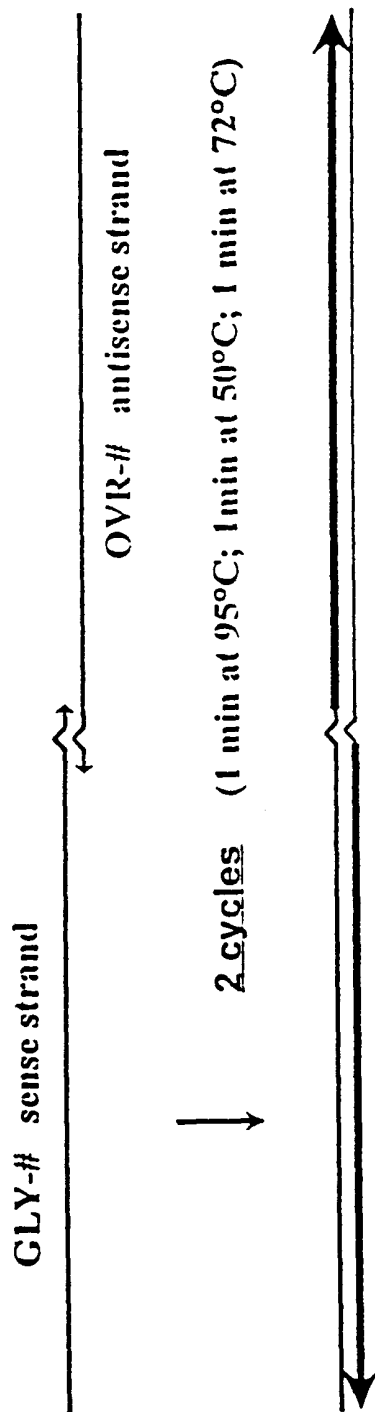


Fig. 42B

2. Overlap extension and nested PCR

a. Overlap extension



b. Nested PCR amplification (GPT-2 and TKr-2 primers)

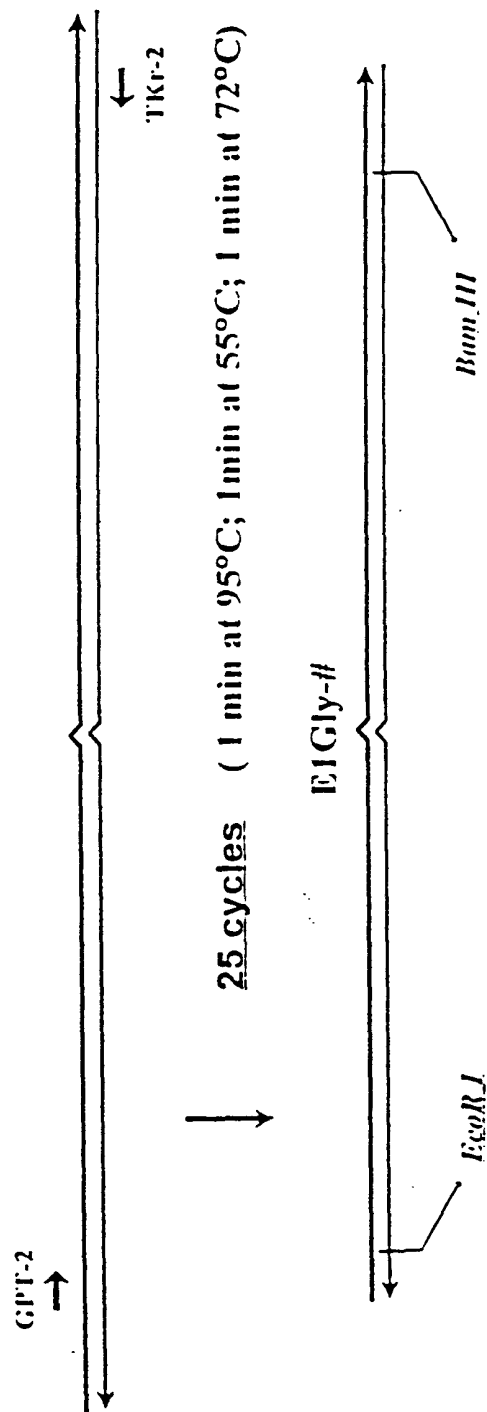
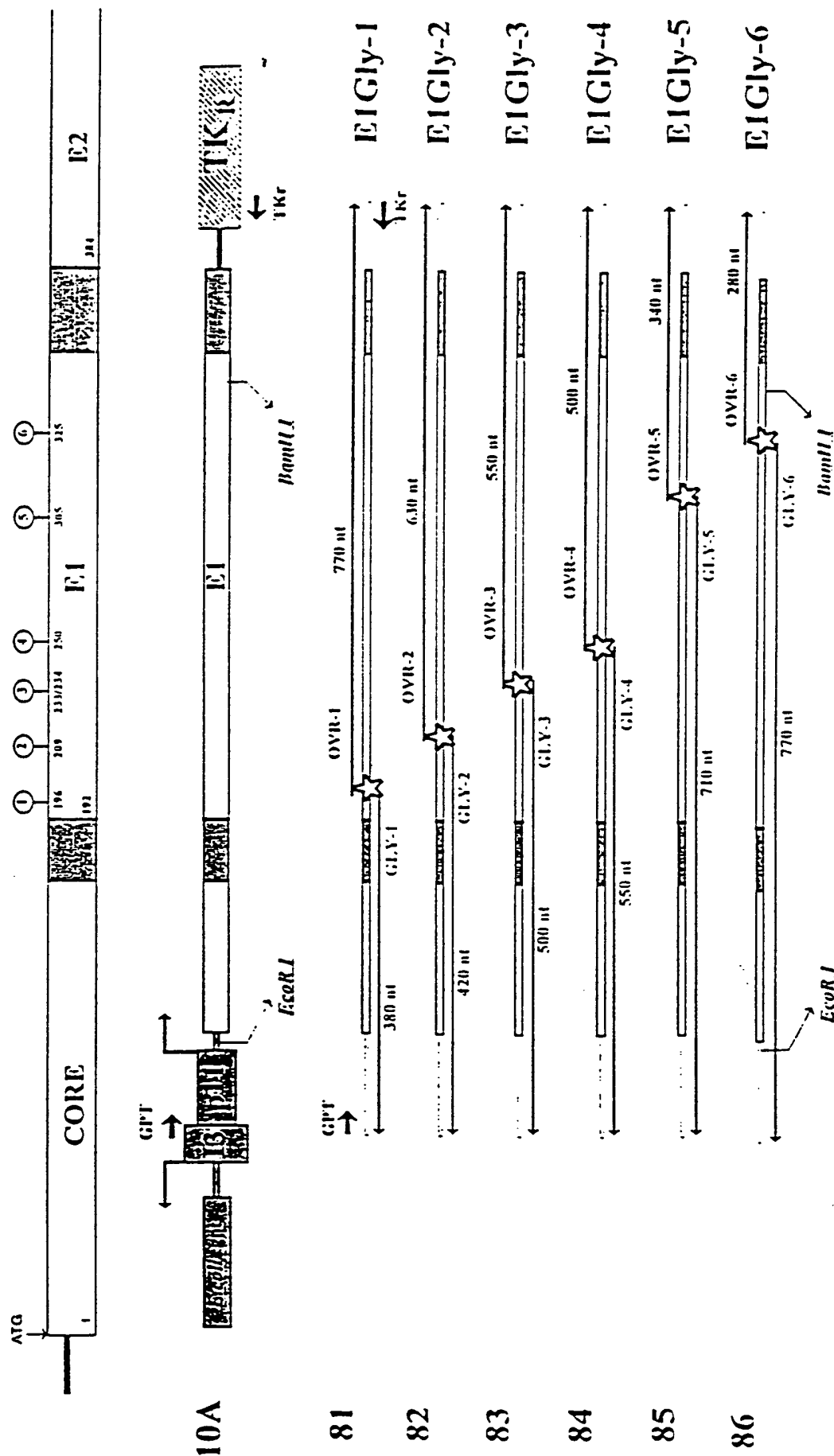


Fig. 43 *In Vitro* Mutagenesis of HCV E1 glycoprotein



		HeLa cells									RK 13 cells									
		1	2	3	4	5	6	7			2	1	3	4	5	6	7	8		
80.0	—								—	80.0									—	80.0
49.5	—								—	49.5									—	49.5
32.5	—								—	32.5									—	32.5
27.5	—								—	27.5									—	27.5
18.5	—								—	18.5									—	18.5

Figure 44A

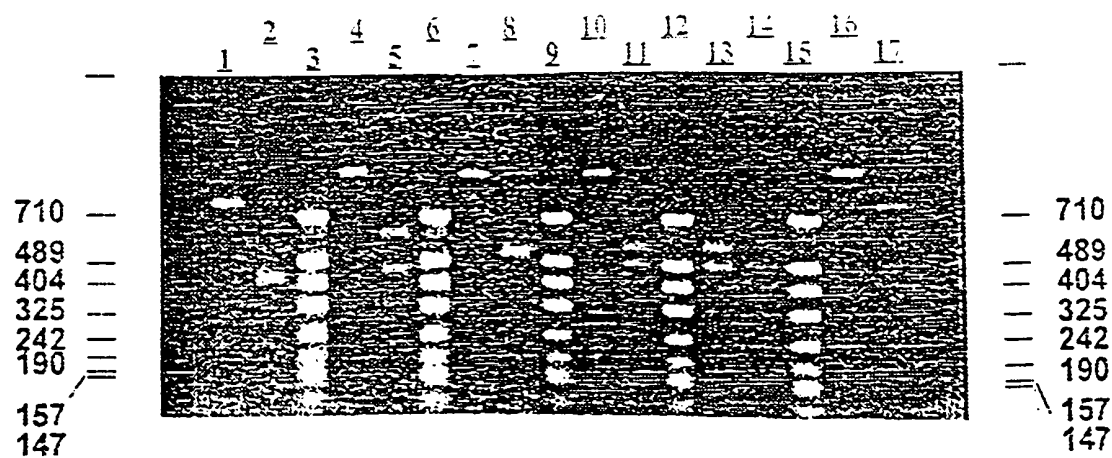


Figure 4-18

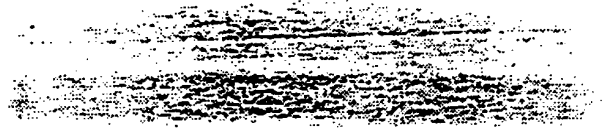


Figure 45

kDa
 — 119
 — 67
 — 43
 — 29
 — 18



Figure 46